POST ASCO MEETING
2026
EDUCATION
BELGIUM

29th Post-ASCO

For Belgium & Luxembourg

SATURDAY MORNING,
20 JUNE 2026
DOLCE LA HULPE, BRUSSELS

Organized under the auspices of the BACR & BSMO:

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PROGRAMME

29th Post-ASCO
20 JUNE 2026

Post-ASCO meeting
Chairs: Dr. Caroline Duhem & Prof. Bart Neyns

08:30	**Registration**
09:00	**Melanoma & non-melanoma skin cancers** *Bart Neyns, UZ Brussel*
09:15	**CNS tumors & Head & Neck** *Pierre Frères, CHU de Liège*
09:30	**Round table discussion 1**
09:50	**Digestive oncology** *Timon Vandamme, UZAntwerp*
10:05	**Thoracic Oncology** *Mariana Brandao, Institut Jules Bordet*
10:20	**Round table discussion 2**
10:40	**Meeting report from Young Investigators (by AstraZeneca)**
	Break
11:20	**Genitourinary cancer** *Sylvie Rottey, UZ Gent*
11:35	**Gynecologic cancer** *Jean Francois Baurain, UC Louvain*
11:50	**Round table discussion 3**
12:10	**Management of Toxicity and Supportive Care** *Sandrine Aspeslagh, UZ Brussel*
12:25	**Breast Cancer** *Laurence Buisseret, Institut Jules Bordet*
12:40	**Round table discussion 4**
13:00	**End of the meeting & Lunch**

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MELANOMA & NON-MELANOMA SKIN CANCERS

Bart Neyns, UZ Brussel

Advances in (neo)adjuvant treatment

Neoadjuvant Management of High-Risk Resectable Melanoma
Professor Georgina Long presented the NeoReNi II phase II trial evaluating neoadjuvant nivolumab (anti-PD-1) plus relatlimab (anti-LAG-3) in resectable stage IIA–IIC cutaneous melanoma. Patients received two pre-operative cycles, followed by surgery at week six. Post-operative management was response-adapted: major pathological responders (MPR) skipped adjuvant therapy, while non-responders received eleven adjuvant cycles. The regimen yielded a 60% pathological complete response (pCR) and 65% MPR rate without delaying surgery. No Grade 4/5 toxicities occurred, demonstrating that brief neoadjuvant dual-checkpoint blockade safely spares responders from long-term adjuvant side effects. The ongoing NeoIRENIE phase II trial is evaluating intensified combinations tailored by multi-omic biomarkers for poor-prognosis cohorts.

A phase II study of neoadjuvant ipilimumab-nivolumab-relatlimab combination immunotherapy in high-risk resectable melanoma
Dr. Ahmad Tarhini presented the NeoINR phase II study evaluating a neoadjuvant triplet—ipilimumab (anti-CTLA-4), nivolumab, and relatlimab (INR)—for macroscopic, resectable stage IIIB–IV melanoma to overcome anti-PD-1 resistance. Among 22 patients, the triplet achieved a 66.7% objective response rate (ORR). Out of 19 surgical patients, the MPR rate was 73.7% and the pCR rate was 63.2%. At 10.3 months median follow-up, the 1-year event-free survival (EFS) was 95.5%, facilitating structural preservation. However, toxicity was severe: 36% skipped cycle two due to Grade >2 adverse events. Grade 3 colitis and rash each occurred in 9.1%, and one patient died from Grade 5 myocarditis. An expansion cohort is underway.

Individualized neoantigen therapy intismeran autogene (intismeran) plus pembrolizumab (pembro) in resected melanoma: 5-year update of the KEYNOTE-942 study
The 5-year analysis of the phase IIb KEYNOTE-942 trial evaluated individualized mRNA neoantigen therapy (INT; intismeran autogene) plus pembrolizumab versus pembrolizumab alone in resected, high-risk stage III/IV melanoma. At 60.3 months median follow-up, the combination significantly reduced the risk of recurrence or death by 49% (5-year RFS: 68.8% vs 49.1%) and distant relapse by 59%. Five-year overall survival (OS) showed a positive trend (92.2% vs 71.3%). Benefits were uniform across all subgroups. The vaccine did not increase immune-related toxicity; events were primarily transient Grade 1/2 injection-site or systemic reactions. INT significantly accelerated T-cell clonal expansion. A global clinical program, including the phase III INTerpath-001 trial, is ongoing.

Neoadjuvant Cemiplimab in Hedgehog Inhibitor-Naïve Basal Cell Carcinoma of the Head and Neck
A phase II multicenter study evaluated neoadjuvant cemiplimab (anti-PD-1) in 35 adults with hedgehog inhibitor-naïve, resectable locally advanced basal cell carcinoma (LA BCC) of the head and neck. Cemiplimab met its primary endpoints, achieving an ORR of 60.1%, a disease control rate (DCR) of 91.4%, and a combined mPR/pCR rate of 28.1%. This tumor downsizing resulted in a surgical benefit rate of 42.9%, allowing for conservative organ preservation (e.g., avoiding orbital exenteration). Cemiplimab was highly tolerable, with treatment-related adverse events (TRAEs) occurring in 35.3% of patients.

Update of Long-Term Efficacy (5-Year Update of the phase II/III RELATIVITY-047 trial), Safety, and Comparative Outcomes of Dual Checkpoint Inhibition in Advanced Melanoma
The phase II/III RELATIVITY-047 trial established frontline fixed-dose nivolumab plus relatlimab (NIVO + RELA) as a benchmark for advanced melanoma. At 5 years, NIVO + RELA demonstrated a significant survival advantage over nivolumab monotherapy, reducing the risk of progression by 21% ($\text{HR} = 0.79$) and melanoma-specific mortality by 29% ($\text{HR} = 0.71$). Survival curves widened progressively over time. Patients with baseline PD-L1 < 1% or LAG-3 resistance markers experienced enhanced benefits. No late-onset toxicities emerged. An indirect treatment comparison (ITC) using propensity-score weighting matched 5-year data from RELATIVITY-047 and CheckMate 067 (NIVO + IPI), demonstrating therapeutic parity between NIVO + RELA and NIVO + IPI, but showing significantly lower Grade 3/4 toxicities with NIVO + RELA.

Advanced cellular therapies for advanced pretreated melanoma

Dr. Marco Donia discussed adoptive cellular therapies, noting that standard bulk tumor-infiltrating lymphocyte (TIL) therapy (lifileucel) delivers a ~30% response rate post-anti-PD-1 failure but is restricted by intensive ICU monitoring, manufacturing times, and high-dose systemic IL-2. Next-generation TILs use selective clonal propagation, CRISPR-mediated PD-1 knockouts, and membrane-bound IL-15 (mbIL15) to eliminate systemic IL-2. Additionally, T-cell receptor (TCR) T-cell therapies modify peripheral T cells to target intracellular antigens like PRAME, avoiding on-target, off-tumor toxicities. CAR-T cell therapy remains exploratory in solid tumors due to a lack of homogeneous surface targets.

OBX-115 engineered tumor-infiltrating lymphocyte (TIL) cell therapy with regulatable membrane-bound IL15 (mbIL15) in patients with advanced melanoma that has progressed on/after immune checkpoint inhibitors
Dr. Allison Betof presented the Agni-01 phase I/II trial of OBX-115, an autologous TIL therapy featuring a regulatable mbIL15 construct stabilized by oral acetazolamide (ACZ). This completely removes the need for systemic IL-2. In 15 heavily pretreated patients (93% post-dual checkpoint failure), the outpatient-compatible platform achieved an ORR of 67% (13% CR, 53% PR) and a 93% DCR. Responses occurred rapidly, and median response duration was not reached at 16.9 months. Responders showed rapid ctDNA clearance. Safety was highly differentiated: there were zero dose-limiting toxicities, zero ICANS, and zero ICU transfers. Grade 3 cytokine release syndrome occurred in only 7% of patients.

Precision Targeting of Intracellular Antigens in patients with uveal melanoma and other melanoma subtypes: Anzutresgene Autoleucel
The phase I/II IMA203-101 trial evaluated anzutresgene autoleucel (anzu-cel), a PRAME-targeted TCR T-cell therapy restricted to the HLA-A02:01 complex. In 33 heavily pretreated patients across multiple melanoma subtypes (including 16 uveal), anzu-cel achieved an ORR of 56% and a DCR of 91%. The median progression-free survival (PFS) was 6.1 months, and median OS was 16.2 months. Durable responses extending past 3 years occurred across metastatic sites, including immunologically "cold" uveal melanoma. Anzu-cel demonstrated a manageable safety profile, supporting the ongoing randomized phase III SUPRAME registration trial.

Advances in the treatment of metastasized uveal melanoma

Darovasertib in combination with crizotinib in first line HLA*A2:01-negative metastatic uveal melanoma, a potential new standard of care
The phase II/III OptimUM-02 trial randomized 313 treatment-naïve, HLA-A02:01-negative metastatic uveal melanoma patients to receive either oral darovasertib (PKC inhibitor) plus crizotinib

(cMET inhibitor) or investigator's choice (predominantly ipilimumab plus nivolumab). The targeted triplet combination significantly improved median PFS to 6.9 months versus 3.1 months for the control ($\text{HR} = 0.42$). The ORR was 37.1% versus 5.8%, and the DCR was 73.3% versus 31.1%. Benefits were consistent across subgroups; OS data are immature. Severe Grade 3/4 TRAEs occurred in 40.6% of the combination group (comparable to 37.0% in controls). Toxicity-related discontinuations were remarkably low (2.5% for darovasertib), establishing this combination as a potential new frontline standard of care.

TIL Therapy in Refractory Metastatic Uveal Melanoma
A phase II trial evaluated autologous TIL Adoptive Cell Therapy (TIL-ACT) in 33 heavily pretreated, highly refractory metastatic uveal melanoma patients with extensive liver involvement. The regimen was well-tolerated and achieved an ORR of 22% with a durable median response duration of 17.3 months. Efficacy was driven by product potency: patients receiving verified tumor-reactive TILs achieved an ORR of 37% versus 0% for non-reactive TILs. Investigators validated the Uveal Melanoma Immunogenomic Score (UMIS); patients with High UMIS (≥ 0.257) achieved a clinical ORR of 44% compared to 8% in the Low UMIS group, demonstrating a 92% negative predictive value.

Adjuvant Immunotherapy in Resected Merkel Cell Carcinoma: STAMP and ADAM Trials

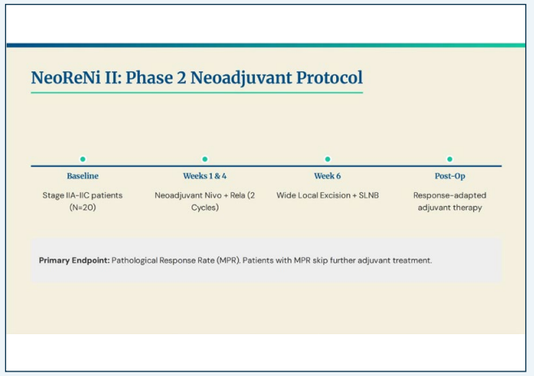
Two phase III trials evaluated adjuvant anti-PD-(L)1 therapy in Merkel cell carcinoma (MCC) following surgery or radiation.

- **STAMP (EA6174)**: Randomized 293 patients (stages I–IIIb) to adjuvant pembrolizumab or observation. Pembrolizumab showed a strong numerical trend toward improved RFS (12-month RFS: 83% vs 72%) and significantly prolonged distant metastasis-free survival (DMFS). Sequential radiation prior to immunotherapy yielded superior benefits.

- **ADAM Trial**: Randomized 100 node-positive stage III patients to avelumab or placebo. Avelumab halved the risk of MCC relapse (age-adjusted $\text{HR} = 0.47$) and improved 1-year RFS by an absolute 27.6%.

Both regimens matched known safety profiles. Given exceptional disease-specific survival (~92%), close clinical surveillance with salvage therapy at relapse remains a safe alternative to mandatory adjuvant therapy.

Real-World Neoadjuvant Immunotherapy (NeoIO) in Merkel Cell Carcinoma
A retrospective Moffitt Cancer Center study analyzed real-world neoadjuvant immunotherapy (NeoIO)—primarily pembrolizumab—in 25 patients with aggressive, resectable MCC. Post-NeoIO, 60% underwent surgery and 16% received radiation. Treatment was well-tolerated (19% Grade 3 TRAEs, 0% Grade 4). NeoIO delivered a 75% ORR. Among 15 evaluable surgical patients, the combined cPR/mPR rate was 60% (40% cPR). At 23.4 months median follow-up, median OS was not reached, showing a significant survival advantage for patients completing regional therapy within 90 days of NeoIO completion.



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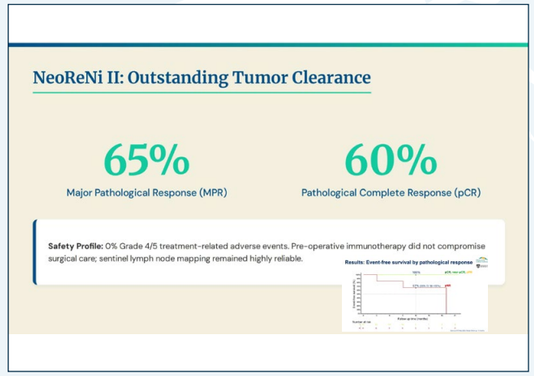

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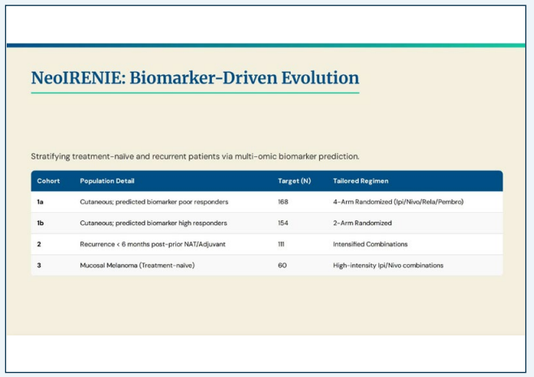

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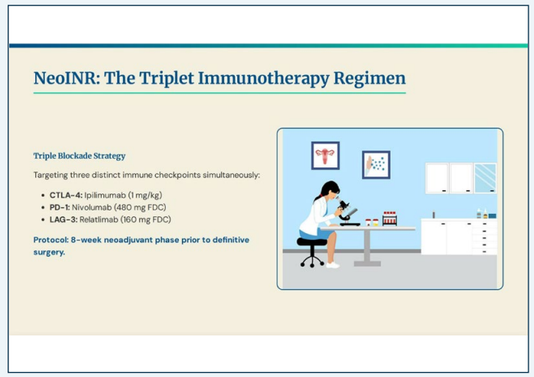

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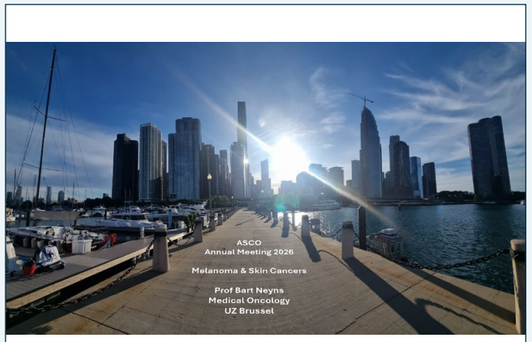

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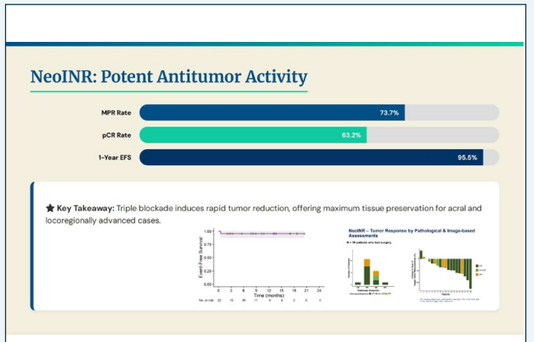

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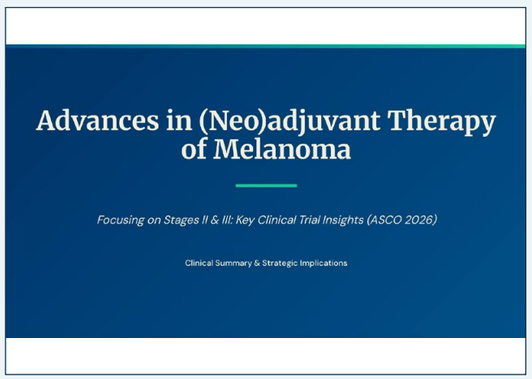

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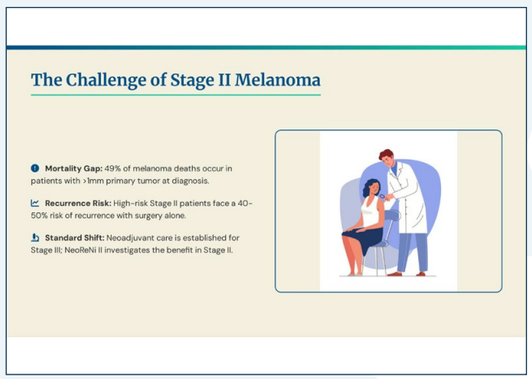

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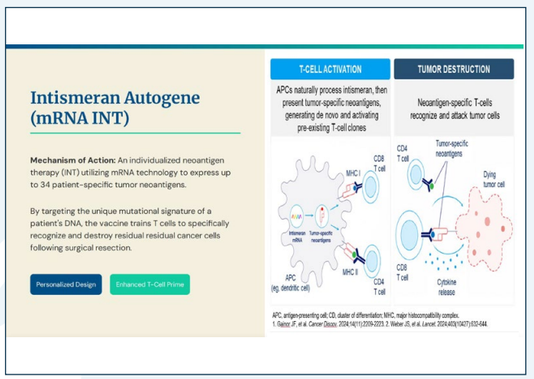

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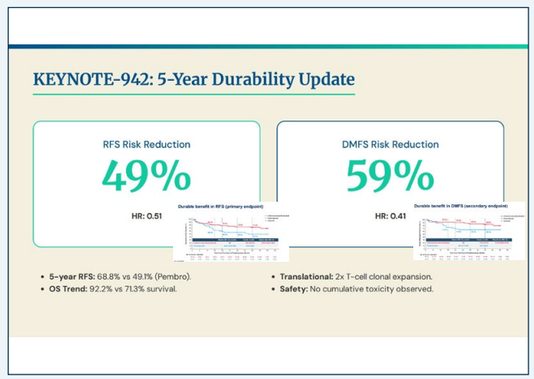

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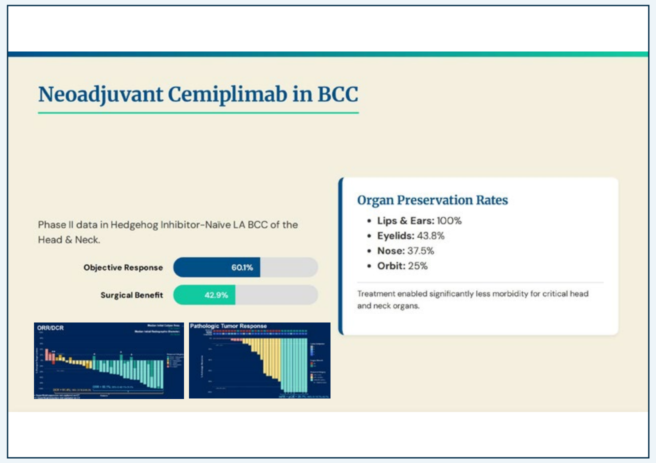

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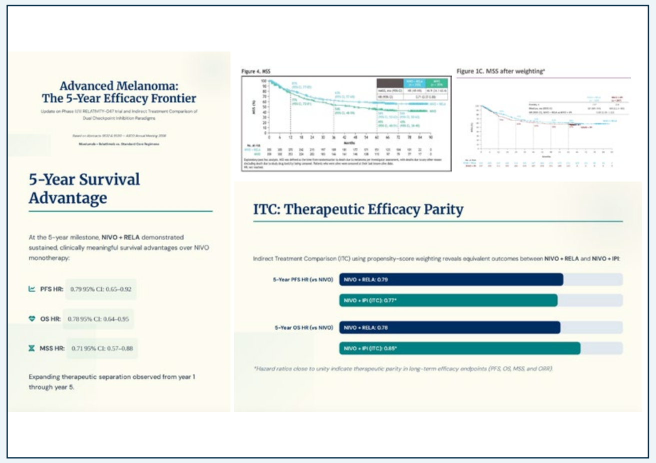

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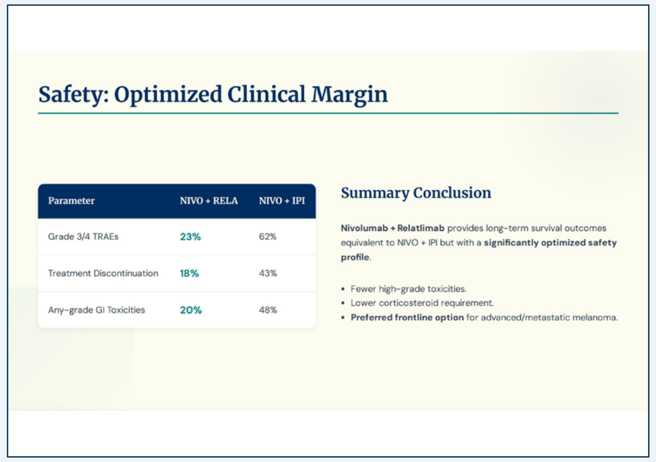

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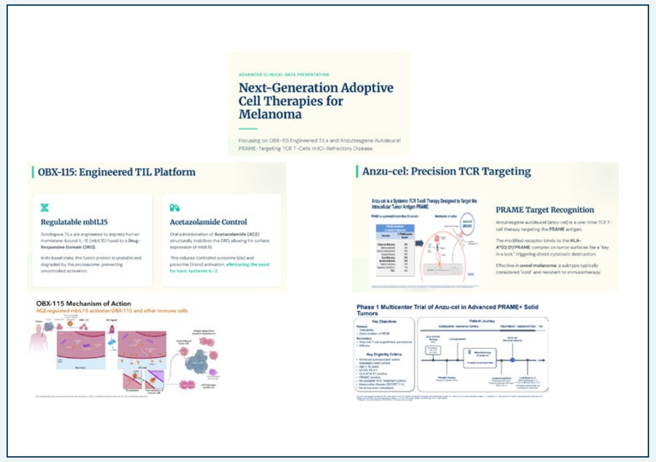

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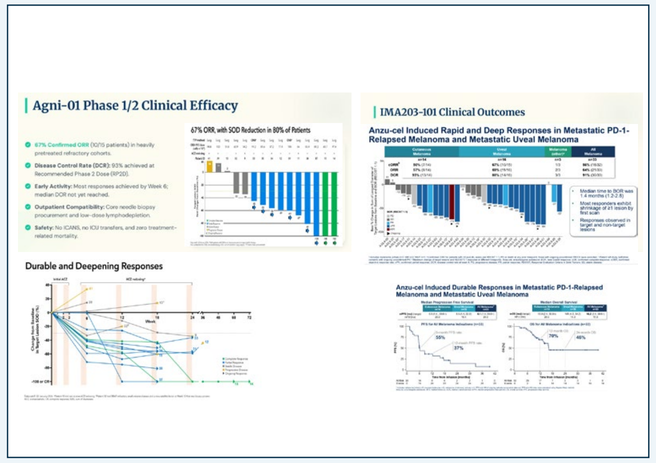

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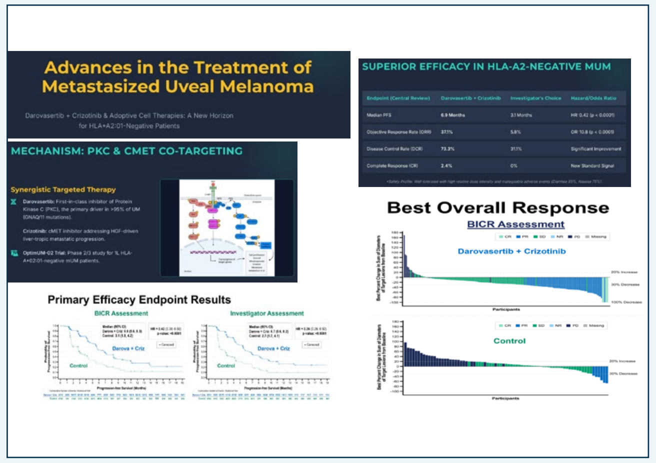

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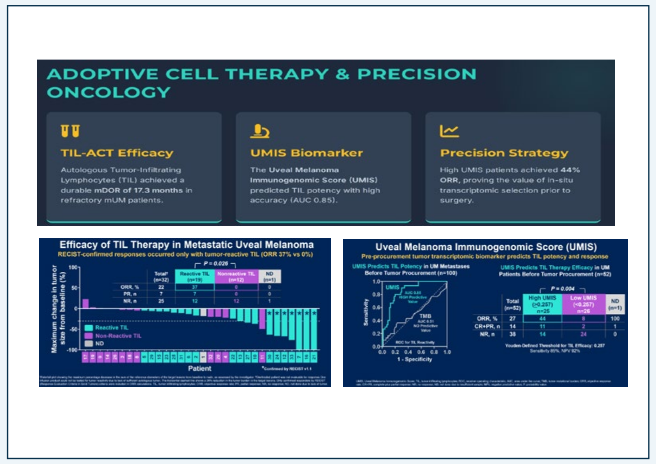

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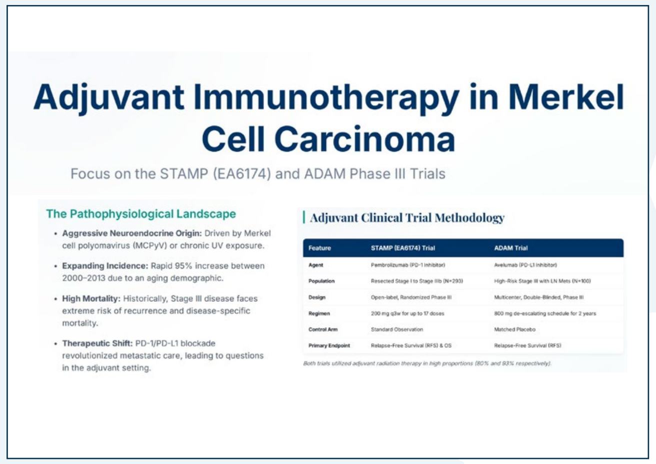

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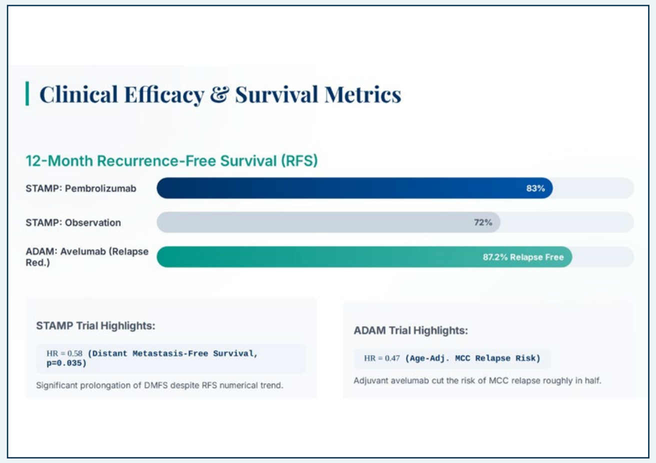

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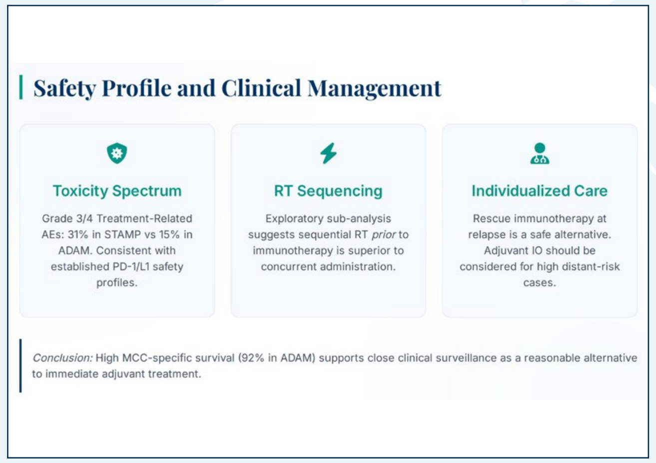

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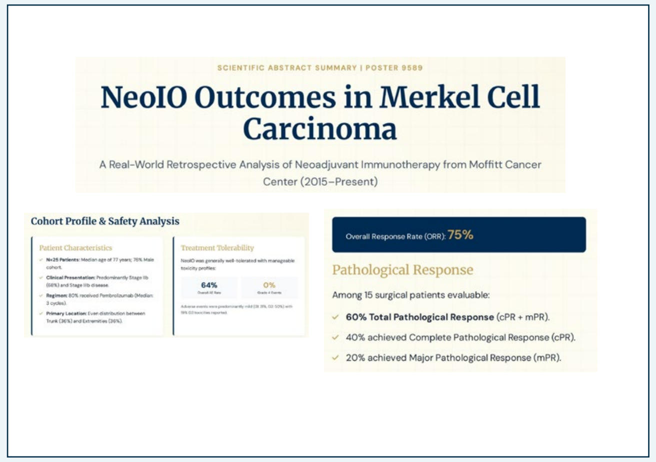

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PATIENTS WITH RECURRENT HEAD AND NECK CANCER: OLD TARGETS, NEW DRUGS

Pierre Frères, CHU de Liège

Recurrent, locally advanced, or metastatic head and neck squamous cell carcinoma (HNSCC) carries a poor prognosis. The introduction of pembrolizumab — either in combination with chemotherapy or as monotherapy — has improved outcomes in this setting. However, long-term follow-up data remain sobering, with 5-year survival rates barely reaching 20%, underscoring the ongoing need for novel therapeutic strategies.

At the 2026 American Society of Clinical Oncology (ASCO) annual meeting, several phase II trials evaluated novel agents in this disease context. Three drugs, already established in other cancer types and targeting molecular alterations long recognized in HNSCC, were of particular interest:

- Amivantamab (bispecific antibody targeting EGFR and MET), administered subcutaneously in the ORIGAMI-4 trial. A total of 102 patients with locally advanced or metastatic HNSCC who had not received prior cetuximab but had progressed after chemotherapy and immunotherapy were enrolled. The objective response rate was 47%, including 15% complete responses. Median time to response was 6 weeks, and half of responses lasted more than 6 months. Responses appeared particularly favorable in oral cavity tumors. These outcomes compare favorably with historical data for cetuximab. A first-line trial combining amivantamab with carboplatin and pembrolizumab is currently recruiting (NCT NCT07276399, the study is open in UZ Antwerpen, Jolimont, UZ Leuven, Vitaz, Institut Roi Albert).
- Trastuzumab deruxtecan (T-DXd), an HER2-targeting antibody-drug conjugate, is especially relevant in salivary gland cancers (SGC), where HER2 overexpression occurs in approximately half of cases. In the MYTHOS trial, enrolling SGC patients with variable HER2 expression levels, a prior report showed a nearly 70% response rate in HER2 3+ or 2+ tumors. New data presented at ASCO 2026 revealed a response rate exceeding 40% in HER2 1+ tumors — though this benefit was observed exclusively in salivary duct carcinoma histology.
- Ivonescimab (bispecific antibody targeting VEGF and PD-1) was tested in the neoadjuvant setting for stage III–IVA HNSCC, combined with platinum-based chemotherapy. Among 35 patients, all but one responded, yielding a pathological complete response rate of 50%. This enabled R0 resection and a high rate of larynx preservation. Surgical complications — including wound healing issues and fistulas — occurred within expected historical ranges, though prospective evaluation is warranted.

These findings highlight a growing trend toward targeted therapies in HNSCC. Other notable data included impressive results with darolutamide plus androgen deprivation therapy in adenoid cystic carcinoma patients. Collectively, these studies underscore the increasing need for comprehensive molecular profiling to identify patients eligible for novel agent trials.

Finally, a major challenge common to all these studies remains the difficulty of enrolling HNSCC patients. Well-recognized barriers include comorbidities, socioeconomic challenges, and overly restrictive eligibility criteria. Rethinking trial inclusion criteria to avoid systematically excluding these patients from clinical research is an urgent priority.

Patients with brain metastases: the ROADS trial

Central nervous system (CNS) tumors continue to present formidable clinical challenges, particularly in the management of resectable brain metastases and the evolving treatment landscape for IDH-mutated gliomas. Despite advances in systemic therapy, brain metastases remain a devastating and frequently underestimated entity, characterized by a median overall survival (OS) of approximately 16 months and a substantial burden of corticosteroid dependency. The current standard of care—postoperative stereotactic radiotherapy (SRT) or stereotactic body radiotherapy (SBRT)—is limited by two critical flaws. First, logistical constraints, including delayed postoperative recovery and scheduling conflicts, result in nearly 20% of patients never receiving the intended radiation. Second, among those treated, local recurrence at the surgical site occurs in roughly 25% of cases despite protocol-conforming radiotherapy.

In response to these limitations, the ROADS phase III trial (Weinberg et al., 2026) offers a potential paradigm shift by comparing Cesium-131 Tile Brachytherapy (TBRT), whereby radiation seeds are embedded in collagen tiles placed directly into the resection cavity, against conventional postoperative SRT. The study randomized 230 patients (204 in the modified intention-to-treat population) presenting with one to six total brain metastases, with a focus on a dominant, resectable index lesion measuring 2.0 to 7.0 cm. In the experimental arm, patients received GammaTiles at the index lesion bed intraoperatively, with SRT reserved for non-index or newly emergent lesions; the control arm underwent standard postoperative SRT to the index lesion and all other sites. The primary endpoint, time-to-surgical bed recurrence (SBR), was not reached in the TBRT arm, whereas the median time-to-SBR in the SRT arm was 17.4 months. At 12 months, the cumulative incidence of SBR was 1.3% with TBRT versus 15.4% with SRT. Most notably, the TBRT arm demonstrated a significant survival advantage, with a median OS of 42.5 months compared to 17.6 months in the SRT arm (hazard ratio 0.59, p=0.032), and 24-month OS estimates of 61.7% versus 35.7%, respectively. This survival benefit is plausibly attributed to the elimination of postoperative treatment delays: the median gap from surgery to SRT in the control arm was 27 days, and prior evidence suggests that each four-week delay in cancer therapy increases the risk of death by approximately 10% (Hanna et al., BMJ 2020). Nevertheless, caution is warranted. The ROADS trial was not placebo-controlled, and outstanding questions remain regarding potential imbalances between arms, as well as infectious and neurocognitive risks associated with implanted radioactive seeds. Moreover, TBRT is not currently available in Europe, which materially limits its immediate applicability to regional practice.

Patients with IDH-mutated glioma: updates from the INDIGO trial

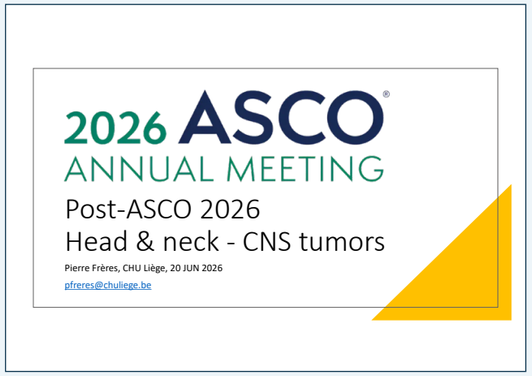
The long-term analysis of the phase III INDIGO trial consolidates the role of vorasidenib as a transformative targeted therapy for patients with IDH-mutated grade 2 gliomas. With a median follow-up of 41.6 months—representing more than three years of extended observation—the updated findings demonstrate durable and sustained clinical benefits that continue to improve over time.

The primary efficacy endpoint, median progression-free survival (PFS), reached 44.1 months in the vorasidenib arm, a marked extension compared to the 11.1 months initially reported for placebo. Furthermore, the median time to next intervention (TTNI) remained not estimable in the vorasidenib group, as only 23.8% of treated patients required subsequent anticancer therapy, underscoring the agent's ability to defer the need for more aggressive interventions such as radiotherapy and chemotherapy. Objective response rates rose to 20.8%, with an additional 72.6% of patients achieving stable disease, indicating that over 90% of vorasidenib-treated patients experienced disease control.

Exploratory analyses from the INDIGO trial also offer clinically relevant insights into seizure control, an important quality-of-life issue for patients with low-grade gliomas. Updated results showed a 72% reduction in seizure rates with vorasidenib compared with placebo. In a model-based analysis, the estimated seizure rate was 18.2 per person-year with vorasidenib versus 51.2 with placebo, corresponding to a rate ratio of 0.36 (95% confidence interval, 0.14–0.89; p=0.0263). These findings suggest that, beyond the effect of tumor shrinkage, IDH inhibition may also have a direct anticonvulsant effect, possibly through lowering levels of the oncometabolite 2-hydroxyglutarate (2-HG), which has been linked to neuronal hyperexcitability.

The extended follow-up confirms that vorasidenib maintains a manageable safety profile consistent with prior reports. Adverse events were predominantly low-grade, with the most common grade 3 or higher toxicities being asymptomatic elevation of alanine aminotransferase (ALT, 10.8%) and aspartate aminotransferase (AST, 4.8%). Fewer than 5% of patients discontinued treatment due to adverse events, and no treatment-related deaths occurred.

Building upon this foundation, the next phase of glioma management is being defined by the EORTC VIGOR trial (NCT06809322), which investigates Vorasidenib as maintenance therapy specifically for patients with grade 2 or 3 astrocytoma who have successfully completed initial radiochemotherapy. This initiative marks a conceptual transition from the traditional "watch-and-wait" approach to an active post-treatment maintenance strategy, with the goal of prolonging disease control.



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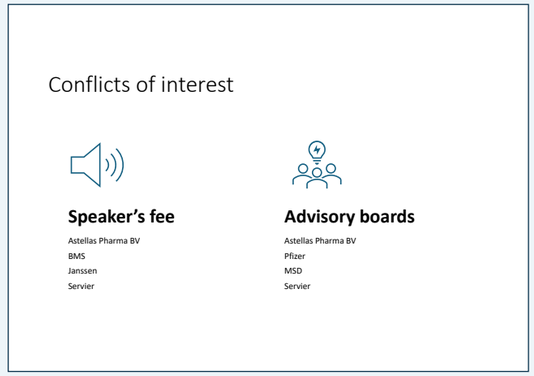

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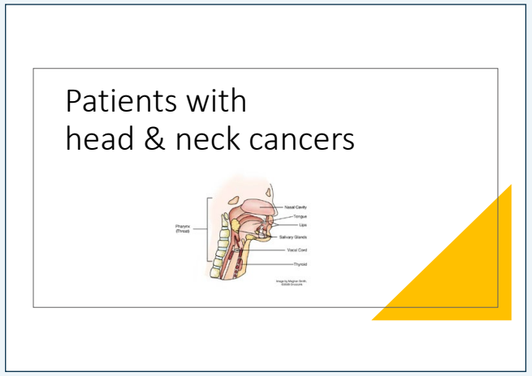

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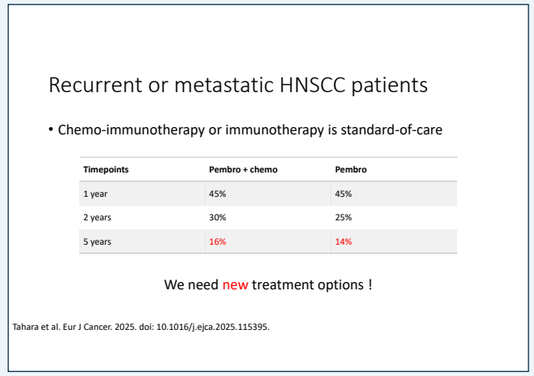

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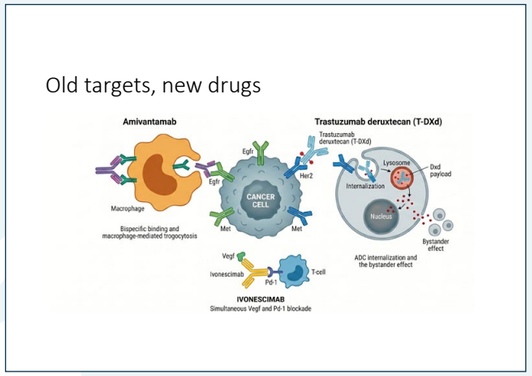

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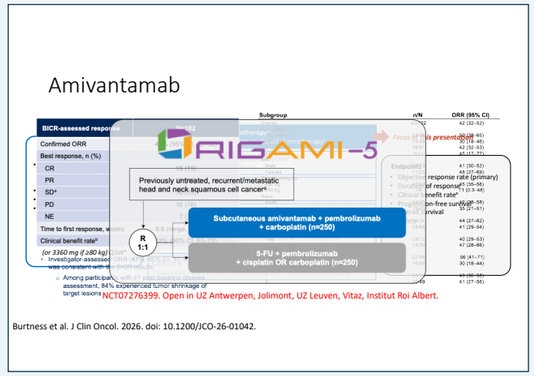

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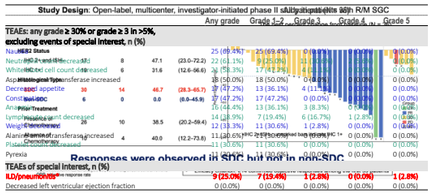
Trastuzumab deruxtecan (T-Dxd) in SGC



Kinoshita et al. 2026 ASCO meeting. Abstract 6011. SGC : salivary gland cancer.

7

Ivonescimab in neoadjuvant setting

Endpoints	
ORR	97.1% (34/35)
cCR, n (%)	20 (57.1%)
PR, n (%)	14 (40.0%)
SD, n (%)	1 (2.9%)
Organ preservation rate (larynge / hypopharyngeal Cancers)	92.6% (25/ 27)

Organ preservation rate & R0 resection rate

- Larynx preservation rate with laryngeal / hypopharyngeal cancers was 92.6%
- Patients who underwent surgical resection achieved a 100% R0 resection rate

Yang et al. 2026 ASCO meeting. Abstract 6014.

8

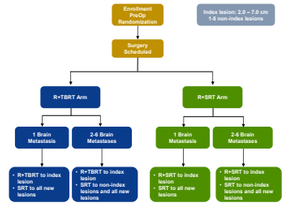
ROADS, phase III, trial

Primary outcomes

Time-to-surgical bed recurrence (time-to-SBR)
Surgical bed recurrence-free survival (SB-RFS)

Secondary outcomes

Overall survival (OS)
Functional status (KPS, Barthel-ADL)
Quality of life (FACT-Br)
Adverse events (AEs)
Development of leptomeningeal disease (LMD)
Assessment of radiation necrosis (RN)
Factors that cause delays in SRT



Weinberg et al. 2026 ASCO meeting. Abstract LBA2000. SBR : surgical bed recurrence.

15

Patients' population

Parameter	R+TBRT	R+SRT
Randomized Patients (Total 230)	115	115
Modified Intent-to-Treat Population (Total 204)	103	101
Median age in years (range)	64 (34, 89)	63 (31, 89)
Sex, M:F	40:63	52:49
Race, %: White, Black, Asian, other/unknown	85.4 | 8.7 | 0.0 | 5.9	80.2 | 13.9 | 2.0 | 4.0
Duration of extracranial disease ≤ 3 months, %	52.4	54.5
Median resected tumor diameter, cm (range)	3.20 (2.0–6.1)	3.25 (2.1–5.8)
Mean number of brain metastases (standard dev)	1.8 (1.13)	1.8 (1.23)
Number of brain metastases, %: 1 | 2-3 | 4-6	58.3 | 34.0 | 7.8	55.4 | 33.7 | 10.9
Extent of Resection, %: GTR | NGTR | STR | unknown	73.8 | 11.7 | 1.9 | 12.6	71.3 | 11.9 | 1.0 | 15.8

Histology	R+TBRT (%)	R+SRT (%)
Lung	43.7	45.5
Melanoma	14.6	10.9
Breast	12.6	8.9
Renal	4.9	5.0
Colon	2.9	5.9
Other	21.4	23.8

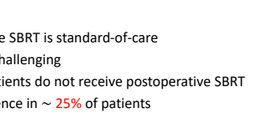
R+SRT Arm	
Fractions: 1 | 3-5	7.8% | 92.2%
Median days from resection to SRT	27 (6–47)
Reasons for SRT delay	rehabilitation, weather events, scheduling

! 20% of patients didn't receive assigned postoperative SBRT !

Weinberg et al. 2026 ASCO meeting. Abstract LBA2000.

16

Discussion



- Targeted therapies are coming in HNSCC
  - EGFR, VEGF, HER2
  - But also, androgen-receptor pathway, B7-H4, NTRK, …
- Extensive molecular profiling for eligible patients

Alsahafi et al. Cell Death Dis. 2019. doi: 10.1038/s41419-019-1769-9.

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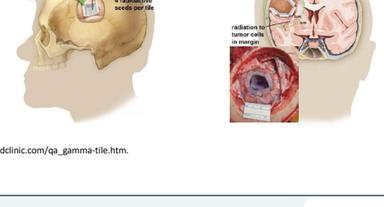
"In H… insuf…



Haddad et al. Oral Oncol. 2015. doi: 10.1016/j.oraloncology.2014.12.007. Chen et al. The Permanent Journal. 2026. doi: 10.7812/TPP/25.219.

10

Primary end-points

Time-to-SBR = time from surgery to SBR

Median time-to-SBR was not reached in R+TBRT vs 17.4 months in R+SRT

12-month cumulative incidence of SBR was 1.3% in R+TBRT vs 15.4% in R+SRT

Weinberg et al. 2026 ASCO meeting. Abstract LBA2000.

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Overall survival

OS = time from surgery to death from any cause

Median OS was 42.5 months in R+TBRT vs 17.6 months in R+SRT

Estimated 24-month OS was 61.7% (95% CI: 48.4–72.5) in R+TBRT vs 35.7% (20.2–51.5) in R+SRT

Weinberg et al. 2026 ASCO meeting. Abstract LBA2000. Hanna et al. BMJ. 2020. doi: 10.1136/bmj.m4087.

18

Patients with central nervous system tumors

11

Newly diagnosed brain mets

- Brain mets is a devastating, underestimated, disease
- Median OS of maximum 16 months
- High steroid dependency and major impact on QoL

- Neurosurgery is sometimes required
  - Symptomatic relief
  - Histologic analyses

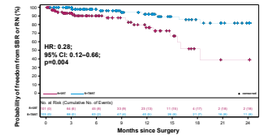
Sperduto et al. J Clin Oncol. 2020. doi: 10.1200/JCO.20.01255. QoL : quality of life.

12

Radiation necrosis or SBR

Functional status, quality of life, distant brain failure, adverse events, radiation necrosis and leptomeningeal dissemination rates were similar in each arm

Median time to SBR/RN was not reached (TBRT) vs 18.3m (SRT)



Weinberg et al. 2026 ASCO meeting. Abstract LBA2000.

19

caution

- Not available in Europe
- Not placebo-controlled trial
- Are the two arms (really) well balanced ?
- Infectious risks and cognitive impact ?

Trial for newly diagnosed glioblastoma patients is completed (NCT05342883)

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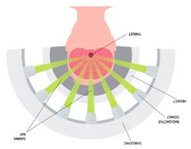

- Postoperative SBRT is standard-of-care
- Logistically challenging
- ~ 20% of patients do not receive postoperative SBRT
- Local recurrence in ~ 25% of patients

Mahajan et al. Lancet Oncol. 2017. doi: 10.1016/S1470-2045(17)30414-X. Chin et al. World Neurosurg. 2020. doi: 10.1016/j.wneu.2020.09.085

13

Cesium-131 based tile therapy (TBRT)

https://mayfieldclinic.com/qa_gamma-tile.htm.

14

INDIGO trial updates

INvestigating vorasiDenIb in GIiOma (NCT04164901)

Key eligibility criteria
- ≥12 years of age
- IDH1/2-mutated* grade 2 oligodendroglioma or astrocytoma per WHO 2016 guidelines
- Prior surgery only
- Measurable non-enhancing disease (≥1 target lesion measuring ≥1 cm × ≥1 cm), confirmed by blinded review
- Not in need of immediate chemotherapy or radiotherapy per investigator assessment

1:1 double-blind randomization (N=331)

Stratified by 1p19q status and baseline tumor size

Vorasidenib 40 mg (N=168)

Orally, once daily, 28-day cycles

Placebo (N=163)

Centrally confirmed progressive disease permitted unblinding and crossover†

IDMC regularly reviewed safety and other clinical data, as well as the efficacy data following prespecified interim analyses

Mellinghoff et al. N Engl J Med. 2023. doi: 10.1056/NEJMoa2304194.

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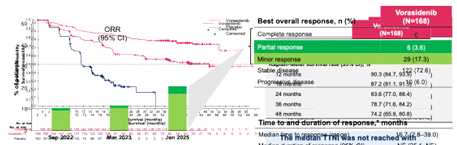
3-years follow-up with vorasidenib



Cloughesy et al. 2026 ASCO meeting. Abstract 2010.

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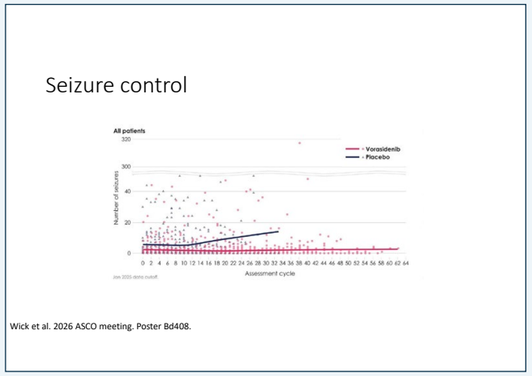

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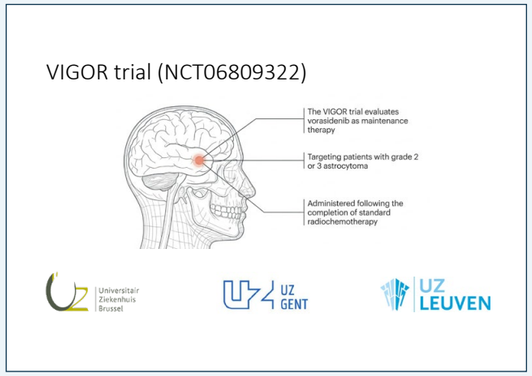

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GI ONCOLOGY AT ASCO 2026: RAS TARGETING ARRIVES, AND PRECISION THERAPY CONTINUES TO RESHAPE THE FIELD

Timon Vandamme, UZ Antwerp[1,2]
[1] Department of Oncology, Antwerp University Hospital (UZA), Edegem, Belgium.
[2] Center for Oncological Research, University of Antwerp, Antwerp, Belgium

Daraxonrasib Changes the Landscape in Pancreatic Cancer
For decades, RAS has been considered the dominant but largely "undruggable" driver of pancreatic cancer. The phase III RASolute 302 trial fundamentally changes that paradigm. Daraxonrasib, an oral multi-selective RAS(ON) inhibitor, significantly improved overall survival, progression-free survival and objective response rate compared with standard chemotherapy in patients with metastatic pancreatic ductal adenocarcinoma (PDAC) after one prior systemic regimen. Median overall survival in the overall population was 13.2 months with daraxonrasib versus 6.7 months with chemotherapy (HR 0.40). Similar benefit was observed in patients with RAS G12 alterations. Progression-free survival improved from 3.5 to 7.3 months, while objective response rate increased from 12% to 33%. Importantly, treatment delayed deterioration in pain and global quality of life. These data establish daraxonrasib as a new standard of care after first-line therapy and represent a genuine breakthrough for pancreatic cancer. Currently, evaluation of Daraxonrasib in first-line is ongoing in multiple phase III trials which will also open in Belgium, both in combination with chemotherapy as in monotherapy. If positive, the field could be moving towards a chemotherapy-free treatment in first-line for PDAC, which of course would be a true revolution in this hard-to-treat disease.

New Directions in Pancreatic Cancer Drug Development
Several early-phase studies suggested future opportunities in pancreatic cancer. Among these, atebimetinib, a cyclic MEK inhibitor, combined with modified gemcitabine and nab-paclitaxel produced encouraging activity, with an objective response rate of 36%, disease control rate of 82%, median progression-free survival of 8.3 months and median overall survival of 17.3 months. Although these findings require confirmation in the ongoing phase III MAPKeeper 301 trial (which will also run in Belgium), they illustrate the continued efforts to move beyond conventional chemotherapy backbones in pancreatic cancer. It is too early to think about potential combination strategies but mechanistically a combination with panRAS inhibition and cyclic MEK inhibition might be interesting.

BRAF V600E Colorectal Cancer: BREAKWATER Establishes a New Standard but no benefit from immunotherapy to encorafenib-cetuximab
The most important colorectal cancer updates centered on molecularly selected populations. First-line phase III BREAKWATER trial solidified the role of upfront BRAF and EGFR inhibition in BRAF V600E-mutated metastatic colorectal cancer. After a positive initial read-out in the FOLFOX cohort, at ASCO 2026 the results in the FOLFIRI cohort were presented with an objective response rates of 66% versus 41%, progression-free survival of 15.2 versus 8.3 months, and an overall survival hazard ratio of 0.56 favoring encorafenib plus cetuximab plus chemotherapy. These findings complemented the previously reported FOLFOX cohort, which showed median overall survival of 30.3 months versus 15.1 months. Taken together, the data strongly support chemotherapy combined with encorafenib and cetuximab as the preferred first-line approach for patients with BRAF V600E-mutant MSS metastatic colorectal cancer. On thecontrary, the SWOG S2107 was negative. This trial investigated the addition of nivolumab to encorafenib and cetuximab in previously treated MSS BRAF V600E-mutant metastatic colorectal cancer. The study failed to improve progression-free survival despite encouraging expectations regarding immune sensitization.

HER2-Positive Colorectal Cancer Enters the ADC Era
HER2-positive colorectal cancer emerged as another area of significant progress. In the randomized phase III HORIZON-CRC01 trial, trastuzumab rezetecan demonstrated a marked improvement in progression-free survival compared with standard later-line therapy.Median progression-free survival improved from 2.8 to 5.5 months (HR 0.33), while objective response rates increased from 4.5% to 40.7%. Although overall survival data remain immature, the magnitude of activity suggests that antibody-drug conjugates are poised to become an important component of treatment sequencing in HER2-positive colorectal cancer. Questions remain regarding optimal sequencing after trastuzumab/tucatinib and trastuzumab deruxtecan, but the therapeutic landscape is clearly evolving.

ctDNA Continues to Mature, but Clinical Utility Remains Unproven
Several presentations focused on circulating tumor DNA (ctDNA), which continues to demonstrate strong prognostic value across colorectal cancer settings. The consistency of the data is increasingly convincing: patients who remain ctDNA-positive after surgery or adjuvant therapy have a substantially higher risk of recurrence, while ctDNA clearance during treatment is associated with more favorable outcomes. This was again illustrated by studies evaluating ctDNA dynamics after adjuvant chemotherapy, as well as by analyses in metastatic colorectal cancer showing that early molecular response can precede and predict radiological benefit.
In KRAS G12C-mutant metastatic colorectal cancer, early ctDNA clearance during treatment with sotorasib plus panitumumab provided further evidence that ctDNA may function as a rapid pharmacodynamic marker of targeted treatment activity. Similarly, in the adjuvant setting, postoperative and post-chemotherapy ctDNA status helped identify patients with very different recurrence risks, potentially allowing future escalation or de-escalation of treatment intensity. These findings support the concept that ctDNA could become a central tool for response monitoring and risk stratification in colorectal cancer.
However, the important distinction between prognostic validity and clinical utility remains as challenge. Although ctDNA clearly identifies patients at high or low risk, no randomized study has yet definitively shown that modifying treatment based on ctDNA results improves survival or recurrence outcomes. Key practical questions also remain unresolved, including the optimal timing of testing, the preferred assay platform, the required sensitivity for minimal residual disease detection, and the best therapeutic intervention for patients who remain ctDNA-positive. Consequently, ctDNA is rapidly becoming one of the most powerful biomarkers in colorectal cancer research, but its routine use to guide treatment decisions should still be considered investigational. For now, ctDNA is best interpreted as a highly informative risk marker and an increasingly useful tool for clinical trial design, rather than as a standalone determinant of adjuvant or metastatic treatment strategy.

Exercise Emerges as a True Adjuvant Intervention
In contrast to ctDNA, the CHALLENGE study continues to provide some of the most compelling adjuvant survivorship data in oncology. Long-term follow-up demonstrated improvements in disease-free survival (HR 0.72) and overall survival (HR 0.63) among patients participating in a structured exercise program following treatment for colon cancer. New health-economic analyses presented at ASCO 2026 further demonstrated that the intervention is highly cost-effective and potentially cost-saving. These findings strengthen the argument that exercise should be viewed as an evidence-based adjuvant intervention rather than simply a lifestyle recommendation. Currently, the question is no longer "should we implement this in the Belgian setting?" but "How fast can we implement this in the Belgian setting?".

Aspirin and Hepatic Arterial Infusion: Two Negative Adjuvant Studies
Two important studies provided negative but clinically relevant findings. The EPISODE-III trial failed to demonstrate a significant disease-free survival benefit for low-dose aspirin in unselected stage III colorectal cancer following surgery and adjuvant chemotherapy. While safety was favorable, the results suggest

that future aspirin strategies should focus on biomarker-selected populations as the result from the ALASCCA trial clearly showed a benefit in a PI3KCA pathway-mutated population. Similarly, the Dutch PUMP trial found no progression-free survival benefit from adjuvant hepatic arterial infusion pump chemotherapy after resection of colorectal liver metastases in low-risk patients. Although technically feasible in European centers, routine implementation cannot currently be recommended.

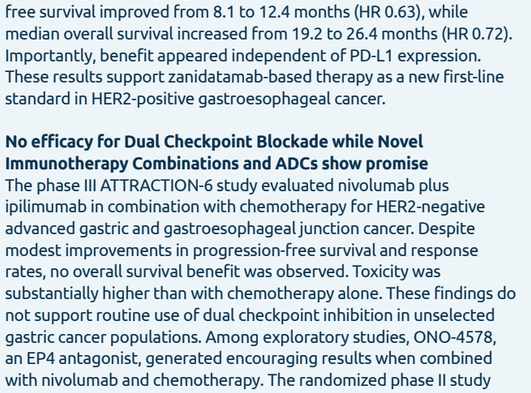
HER2-Positive Gastroesophageal Cancer: A New First-Line Standard
One of the most important gastroesophageal cancer presentations was the HERIZON-GEA-01 update. Zanidatamab combined with tislelizumab and chemotherapy significantly improved outcomes compared with trastuzumab-based therapy in first-line HER2-positive advanced gastroesophageal adenocarcinoma. Median progression-free survival improved from 8.1 to 12.4 months (HR 0.63), while median overall survival increased from 19.2 to 26.4 months (HR 0.72). Importantly, benefit appeared independent of PD-L1 expression. These results support zanidatamab-based therapy as a new first-line standard in HER2-positive gastroesophageal cancer.

No efficacy for Dual Checkpoint Blockade while Novel Immunotherapy Combinations and ADCs show promise
The phase III ATTRACTION-6 study evaluated nivolumab plus ipilimumab in combination with chemotherapy for HER2-negative advanced gastric and gastroesophageal junction cancer. Despite modest improvements in progression-free survival and response rates, no overall survival benefit was observed. Toxicity was substantially higher than with chemotherapy alone. These findings do not support routine use of dual checkpoint inhibition in unselected gastric cancer populations. Among exploratory studies, ONO-4578, an EP4 antagonist, generated encouraging results when combined with nivolumab and chemotherapy. The randomized phase II study demonstrated progression-free survival of 9.0 months versus 6.9 months (HR 0.67), particularly among patients with PD-L1-positive disease. While these findings require phase III validation, they highlight innovative approaches aimed at overcoming resistance to immune checkpoint blockade. In esophageal squamous cell carcinoma, the Chinese phase III PANKU-Esophagus01 trial evaluated the EGFR/HER3 bispecific antibody-drug conjugate izalontamab brengitecan. The study demonstrated significant improvements in both progression-free survival (4.17 vs 1.97 months) and overall survival (9.79 vs 7.20 months) compared with chemotherapy following prior platinum and PD-1-based treatment. Although international validation remains necessary, these data suggest a potentially important future treatment option in refractory ESCC.In neuroendocrine carcinoma, the randomized phase II dose-optimization study of alveltamig (ZG006), a trispecific DLL3/DLL3/CD3 T-cell engager, showed encouraging activity in previously treated NEC patients with DLL3 expression in at least 50% of tumor cells. The 30 mg Q2W dose appeared most active, with a confirmed objective response rate of 56.3%, and a median duration of response of 11.76 months. With approximately 14 months of follow-up, median overall survival had not yet been reached in the 30 mg cohort, and the 12-month OS rate was 75%. These early data further support the role of DLL3 as a promising immunotherapeutic therapeutic target in NEC.

First-Line FGFR Inhibition Advances in Cholangiocarcinoma
The phase III FIGHT-302 trial provided the strongest evidence to date supporting earlier use of FGFR inhibition in FGFR2-rearranged cholangiocarcinoma. Although the trial was halted due to poor recruitment and could therefore not reach its foreseen statistical power, pemigatinib significantly improved progression-free survival compared with gemcitabine-cisplatin (8.34 vs 6.80 months; HR 0.58) and increased objective response rates from 15.5% to 47.0%. While overall survival differences were likely obscured by crossover and early cross-over, the trial confirms the importance of comprehensive molecular profiling at diagnosis and supports consideration of targeted therapy earlier in the disease course.

Balancing Efficacy and Toxicity in Hepatocellular Carcinoma
Several hepatocellular carcinoma studies explored increasingly complex strategies combining immunotherapy, antiangiogenic therapy and locoregional treatment. The main discussion focused on whether the addition of systemic therapy to TACE can meaningfully improve outcomes in patients with embolization-eligible unresectable HCC. The EMERALD-3 trial provided important phase III data in this setting. In patients with unresectable embolization-eligible HCC, STRIDE plus lenvatinib combined with TACE improved progression-free survival compared with TACE alone, with median PFS of 13.1 versus 8.1 months and a hazard ratio of 0.66. STRIDE plus TACE without lenvatinib also improved PFS, with median PFS of 12.9 versus 8.1 months and a hazard ratio of 0.71. Early overall survival analyses were encouraging but not yet definitive. These data suggest that immunotherapy-based TACE combinations may become an important option in selected patients. However, without clear benefit on overall survival, this regimen is not yet ready from prime time. In the advanced-disease setting, IMbrave251 addressed a different but highly relevant question: whether atezolizumab should be continued beyond progression after first-line atezolizumab plus bevacizumab. The trial randomized patients to atezolizumab plus lenvatinib or sorafenib versus lenvatinib or sorafenib alone after prior benefit from atezolizumab/bevacizumab. The study did not meet its primary overall survival endpoint. Median OS was 14.6 months with continued atezolizumab plus TKI versus 12.5 months with TKI alone, with a hazard ratio of 0.88 and no statistically significant benefit. PFS was also not improved, with median PFS of 4.3 versus 4.8 months. IMbrave251 shows that continuing immunotherapy beyond progression is not sufficient as a general strategy.

Conclusions
ASCO 2026 will be remembered in GI oncology for one truly practice-changing presentation: the phase III RASolute 302 trial of daraxonrasib in previously treated metastatic pancreatic adenocarcinoma, which established daraxonrasib as a new standard of care for previously treated metastatic pancreatic cancer and provided the first convincing demonstration that direct RAS inhibition can substantially improve survival in pancreatic ductal adenocarcinoma. In other GI tumor types, progress seems to be focused on molecular selected subgroups such as BRAF V600E-mutant CRC and HER2-positive GEJ-, gastric and colorectal cancer



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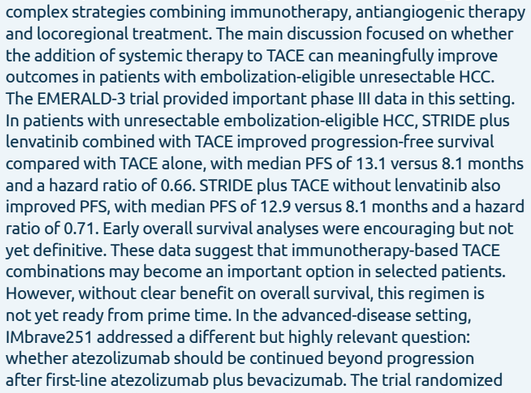

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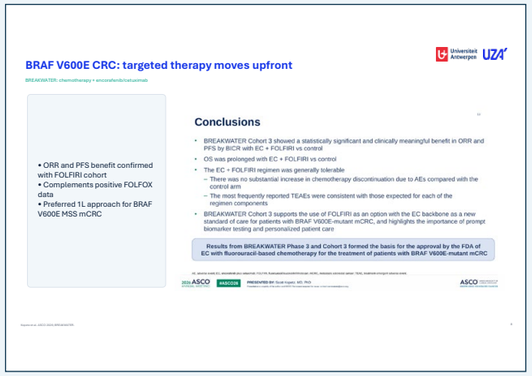

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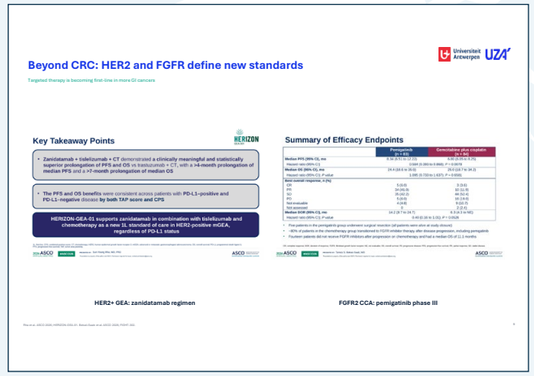

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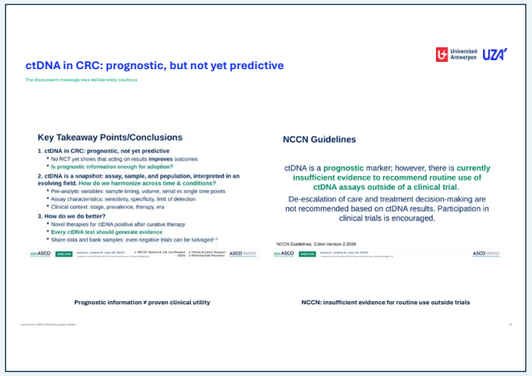

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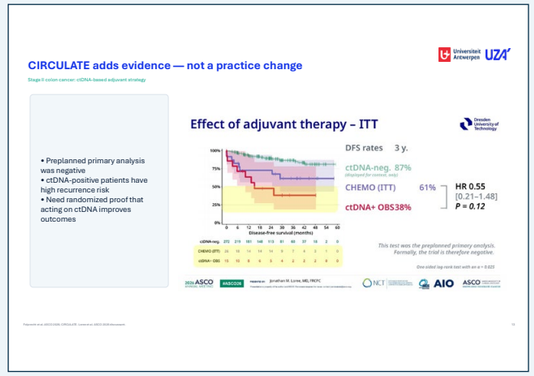

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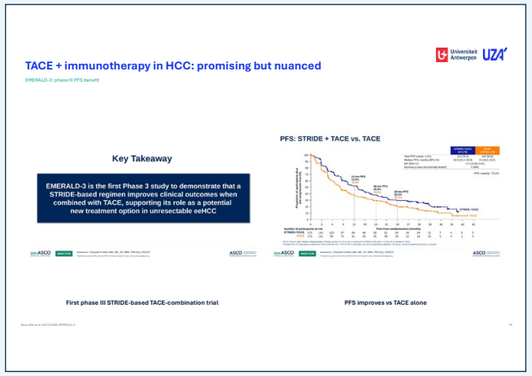

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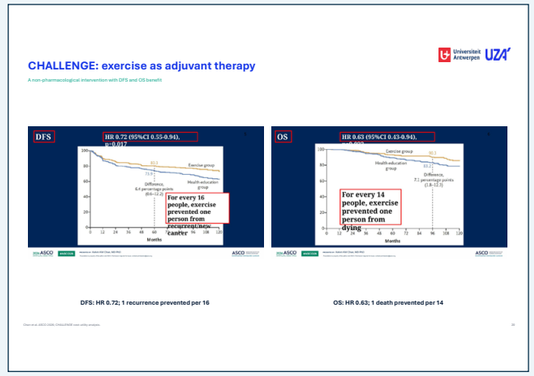

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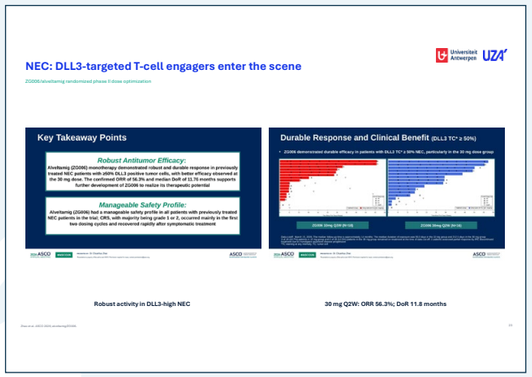

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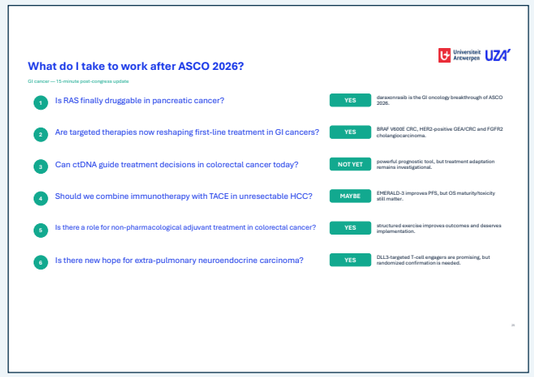

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LATEST ADVANCES IN THORACIC ONCOLOGY AT ASCO 2026

Mariana Brandao, Institut Jules Bordet

ASCO 2026 further refined the therapeutic landscape of non–small cell lung cancer (NSCLC) across both molecularly defined and biomarker-negative populations, highlighting two parallel trends: earlier use of targeted therapies and the expansion of immunotherapy combinations and antibody drug conjugates (ADC)-based strategies.
Key practice-changing data include a marked adjuvant benefit with selpercatinib in early-stage RET fusion NSCLC, positive first-line results for sunvozertinib in EGFR exon 20 insertion disease, and 7-year confirmation of lorlatinib's durable systemic and intracranial control in ALK-positive NSCLC. In contrast, adjuvant nivolumab failed to improve disease-free survival. Novel combinations, such as a PD-1/VEGF bispecific antibody and an ADC plus PD-1 blockade, also showed promising efficacy signals, mainly in Chinese cohorts, warranting global validation.
This overview highlights selected abstracts from ASCO 2026 and is not intended to be comprehensive.

NSCLC with actionable genomic alterations

Adjuvant selpercatinib for RET fusion early NSCLC (LIBRETTO 432)[1]
In early-stage NSCLC, there are already two approved targeted therapies after local treatment: osimertinib for patients with stage IB-IIIA resectable or stage III unresectable NSCLC with classic EGFR mutations and alectinib for ALK fusion positive resected NSCLC. However, until now, there were no targeted therapies approved for patients with other actionable genomic alterations (AGA).
The **LIBRETTO 432 trial** was the first study testing a RET-directed tyrosine kinase inhibitor (TKI) in RET fusion-positive NSCLC. In patients with stage II–IIIA (the intention-to-treat population), three years of adjuvant selpercatinib produced a large improvement in event free survival (EFS): 2 year EFS was 92% versus 61% with placebo (HR = 0.17, 95% confidence interval [CI], 0.06-0.51). In the overall population (stage IB-IIIA), 2 year EFS was 94% with selpercatinib and 70% with placebo (HR = 0.17, 95% CI, 0.06-0.49).
This magnitude of benefit is large and clinically meaningful in a population at substantial risk of recurrence; the result is biomarker driven and immediately actionable where RET testing is available.
However, RET fusions are rare, so sample size was modest (n=151) and overall survival (OS) data remain immature; racial representation was limited in parts of the dataset. Duration of therapy and optimal sequencing with adjuvant chemotherapy also require further refinement.
Practice implications: Routine RET testing in resected stage II–IIIA NSCLC should be prioritized. Adjuvant selpercatinib is now a standard option for eligible patients after multidisciplinary review, with counseling about expected toxicities and the current evidence base.

Sunvozertinib as first line therapy for metastatic NSCLC with EGFR exon 20 insertions (WU KONG28)[2]
EGFR exon 20 insertion mutations occur in 2 to 3% of cases of NSCLC and in up to 12% of cases of EGFR-mutated NSCLC. The insertional mutations at EGFR exon 20 induce a rigid conformation of the kinase-active site and form steric hindrance, an effect that results in a smaller drug-binding pocket and limits effective binding of conventional first- to third-generation EGFR TKIs, such as osimertinib. Thus, until recently, these patients received chemotherapy as first-line treatment and their prognosis is generally poor. The phase III PAPILLON trial showed that the addition of amivantamab (a bispecific anti-EGFR/anti-MET antibody) to chemotherapy with carboplatin-pemetrexed leads to a significant improvement in progression-free survival (PFS). This regimen is approved in Europe, but not reimbursed in Belgium.
The **WU KONG28** trial compared Sunvozertinib, a TKI specifically designed to target EGFR exon 20 insertions, against chemotherapy. Sunvozertinib significantly PFS versus carboplatin pemetrexed (median PFS 10.3 vs 7.5 months; HR 0.65, 95% CI 0.50-0.85) and produced higher objective response rates (58.9% vs 31.1%).
The advantage of Sunvozertinib is that it is an oral, chemotherapy sparing targeted option with broad activity across exon 20 subtypes and durable responses, which improves convenience and may preserve quality of life for many patients.
Nonetheless, higher rates of grade ≥3 adverse events (notably creatine kinase elevations, diarrhea, anemia) require active monitoring and management. OS data are immature and cross over may confound long term comparisons. Also, there is no head-to-head comparison with the current standard-of-care, which is the combination of carboplatin-pemetrexed with amivantamab.
Practice implications: Sunvozertinib is a compelling first line option for patients with confirmed EGFR exon 20 insertions where available; baseline and on treatment monitoring (CK, LFTs, hematologic parameters) and early toxicity management are essential.

Lorlatinib 7 year update (CROWN) — first-line therapy for metastatic NSCLC with ALK fusions[3]
Rearrangements of the anaplastic lymphoma kinase (ALK) gene are found in approximately 4% of NSCLC and confer sensitivity to treatment with ALK TKIs. Lorlatinib is a highly potent third-generation macrocyclic ALK TKI, specifically developed to penetrate the blood-brain barrier and have broad activity against most known ALK resistance mutations.
In the phase 3 **CROWN** study, lorlatinib showed superior efficacy over crizotinib in patients
with treatment-naive advanced ALK-positive NSCLC, with marked PFS benefit and intracranial efficacy.
In this updated analysis, after 7 years of follow up, median PFS remained not reached with lorlatinib versus 9.1 months with crizotinib (HR 0.19), with sustained intracranial control and a 7 year PFS of 55% on lorlatinib. OS follow-up is still ongoing. This unprecedented long-term systemic and intracranial disease control suggests that first-line lorlatinib could transform outcomes for many patients with ALK-positive disease, with the potential to redefine it as a more chronic condition for a significant proportion of patients.
Still, lorlatinib's metabolic and neurocognitive adverse event profile (hyperlipidemia, weight gain, neurological effects) requires proactive management; long term toxicity surveillance and standardized mitigation strategies are needed.
Practice implications: Lorlatinib should be considered the preferred first line ALK TKI, particularly for patients with baseline brain metastases. Clinicians must implement lipid management and neurocognitive monitoring.

Neoadjuvant lorlatinib in stage III ALK-positive NSCLC (LORIN)[4]
While targeted therapies have transformed outcomes in advanced ALK-positive NSCLC and are now established in the adjuvant setting, data on neoadjuvant approaches remain limited. The phase II LORIN trial explored the feasibility and efficacy of neoadjuvant lorlatinib in patients with potentially resectable or initially unresectable stage III ALK-positive NSCLC. Patients received up to three cycles of lorlatinib followed by multidisciplinary evaluation for surgery or other local therapies, with optional consolidation lorlatinib.
Neoadjuvant lorlatinib demonstrated high activity, with an objective response rate of 83.7%. Among the 32 patients who underwent surgery, the R0 resection rate was 96.9%, with major pathological response (MPR) and pathological complete response (pCR) rates of 81.3% and 46.9%, respectively. Notably, 75% of patients initially deemed unresectable were converted to surgical candidates, and nodal downstaging occurred in over 90% of resected cases. At a median follow-up of 13 months, the 1-year event-free survival rate was 97.1%, with no deaths reported. These findings suggest that neoadjuvant lorlatinib may enable deep tumor responses and substantially increase surgical eligibility in locally advanced ALK-positive NSCLC, representing a promising step toward integrating highly potent ALK inhibition earlier in the disease course. However, the single-arm design, limited sample size, and short follow-up warrant caution, and confirmatory randomized studies with longer-term outcomes are needed before routine adoption.
Practice implications: Neoadjuvant lorlatinib should currently be considered investigational, but may be an attractive option within clinical trials or selected multidisciplinary settings, particularly for patients with borderline resectable or initially unresectable stage III ALK-positive disease.

NSCLC without actionable genomic alterations (AGA)

Adjuvant nivolumab after standard adjuvant therapy (EA5142 / ALCHEMIST)[5]
In recent years, the addition of immunotherapy to chemotherapy has transformed the treatment of patients with early-stage resectable EGFR/ALK negative NSCLC. Multiple neoadjuvant, perioperative and adjuvant trials have been presented. Although the added value of immunotherapy in the neoadjuvant / perioperative setting in terms of EFS and OS improvement is well-established, its role in the adjuvant setting is less-well defined.
The large **EA5142 / ALCHEMIST** trial enrolled 935 patients with resected stage IB≥4cm, II or IIIA EGFR/ALK negative NSCLC. However, 1 year of adjuvant nivolumab given after completion of planned adjuvant chemotherapy and/or radiotherapy did not improve disease free survival in the ITT population (median DFS 71.3 vs 68.8 months; HR 0.97, 95% CI 0.81-1.17) nor among patients with PD-L1 high (≥50%) tumors (median DFS 89.9 vs 78.5 months; HR 0.86, 95% CI 0.59-1.25). There were no differences, either, in terms of OS.
Practice implications: This additional negative trial on the use of immunotherapy after surgery reinforces the shift towards the use chemo-immunotherapy preferentially in the neoadjuvant / perioperative setting.

Advanced / metastatic NSCLC without AGA
In Europe, first-line treatment strategies for non–oncogene-addicted NSCLC are largely guided by tumor PD-L1 expression. Patients with PD-L1 expression ≥50% typically receive anti–PD-(L)1 monotherapy or in combination with chemotherapy; those with PD-L1 expression of 1–49% generally receive chemoimmunotherapy; and patients with PD-L1–negative tumors (<1%) may be treated with chemoimmunotherapy or with a combination of nivolumab (anti–PD-1) and ipilimumab (anti–CTLA-4) alongside a short course of chemotherapy.
Although these approaches have substantially improved overall survival in advanced/metastatic NSCLC over the past decade, most patients ultimately experience disease progression and die from their disease. This underscores the need for more effective therapeutic strategies, including novel immunotherapy- and chemotherapy-based approaches.

HARMONi 6 (ivonescimab) — PD 1/VEGF bispecific in advanced squamous NSCLC[6]
Ivonescimab is a bispecific antibody targeting PD-1 and VEGF and it has shown promising efficacy in terms of tumor response and PFS in advanced NSCLC, supported by both phase 2 and phase 3 studies.
In the randomized, double blind phase 3 **HARMONi 6** trial in China, ivonescimab plus chemotherapy improved OS versus tislelizumab (anti-PD-1) plus chemotherapy (median OS 27.9 vs 23.7 months; HR 0.66, 95% CI 0.50-0.87) at interim analysis. This demonstrates that PD 1/VEGF bispecific blockade can add survival benefit over PD 1 alone in squamous histology, a population with historically limited targeted options.
However, the study population was Chinese and predominantly male; safety signals (higher grade ≥3 adverse events and hemorrhage) require careful evaluation. Global generalizability and confirmatory trials are needed.
Practice implications: The regimen is promising and may become a new option for squamous NSCLC pending regulatory review and global validation; clinicians should monitor bleeding risk and other class specific toxicities.

OptiTROP Lung05 (sacituzumab tirumotecan + pembrolizumab) - PD L1 ≥1% NSCLC[7]
In PD L1 ≥1% advanced NSCLC, sacituzumab tirumotecan (a TROP2 directed ADC) plus pembrolizumab significantly prolonged PFS versus pembrolizumab alone (median PFS not reached vs 5.7 months; HR 0.35, 95% CI 0.26-0.47) at interim analysis. This benefit seemed larger among patients with PD-L1 TPS of 1-49% (HR 0.28, 95% CI 0.19-0.41) than among those with PD-L1 TPS of ≥50% (HR 0.47, 95% CI 0.29-0.77).
This trial shows that ADC + PD 1 combinations may improve PFS across PD L1 strata and histologies, offering a new biologic strategy beyond "classic" chemoimmunotherapy.
Nonetheless, interim follow up is short and OS data are pending; grade ≥3 toxicity was higher in the combination arm, necessitating careful patient selection and toxicity management. Also, the trial was conducted in China and requires broader validation.
Furthermore, Pembrolizumab alone as the comparator arm in the PD-L1 TPS of 1-49% is not considered adequate in Europe, where the standard-of-care treatment is chemoimmunotherapy.
Practice implications: ADC + PD 1 is a compelling strategy for PD L1 positive disease; adoption should be guided by regulatory approvals and institutional capacity to manage ADC related toxicities.

Conclusions
ASCO 2026 delivered several practice defining and practice influencing results. Targeted therapies continue to reshape outcomes for molecularly defined NSCLC, while innovative immunotherapy and ADC combinations expand therapeutic possibilities for PD L1 positive and squamous disease. The immediate clinical task is to integrate molecular testing into routine workflows, adopt targeted adjuvant and first line strategies where evidence is robust, and cautiously evaluate novel immunotherapy-based combination regimens as confirmatory data emerge.

References

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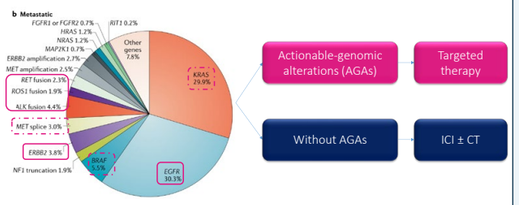
2 *Zhou C, Greillier L, Liu G, et al. First-Line Sunvozertinib in NSCLC with EGFR Exon 20 Insertion Mutations. N Engl J Med; 0. DOI:10.1056/NEJMoa2604461.*
3 *Shaw AT, Solomon BJ, Felip E, et al. Lorlatinib versus crizotinib as first-line treatment for advanced ALK-positive non-small cell lung cancer: 7-year update from the phase 3 CROWN study. Ann Oncol 2026; 0. DOI:10.1016/j.annonc.2026.05.692.*
4 *hang C, Hu Y, Jiang B-Y, et al. Neoadjuvant lorlatinib in stage III NSCLC harboring ALK fusion: A phase 2 multicenter study (LORIN). J Clin Oncol 2026; 44: 8002–8002.*
5 *Chaft JE, Sun Z, Rudin CM, et al. Adjuvant Nivolumab vs Observation in Resected Non–Small Cell Lung Cancer: A Randomized Clinical Trial. JAMA 2026; published online June 1. DOI:10.1001/jama.2026.8992.*
6 *Lu S, Liu B, Luo Y, et al. Ivonescimab plus chemotherapy versus tislelizumab plus chemotherapy in advanced squamous non-small-cell lung cancer (HARMONi-6): interim overall survival analysis of a randomised, double-blind, phase 3 trial in China. Lancet 2026; : S0140-6736(26)00966-9.*
7 *Xiong A, Yao W, Zheng W, et al. Sacituzumab tirumotecan plus pembrolizumab versus pembrolizumab in PD-L1-positive advanced non-small-cell lung cancer (OptiTROP-Lung05): interim analysis of a randomised, open-label, phase 3 trial. Lancet 2026; : S0140-6736(26)00968-2.*

NSCLC is *not* a single disease

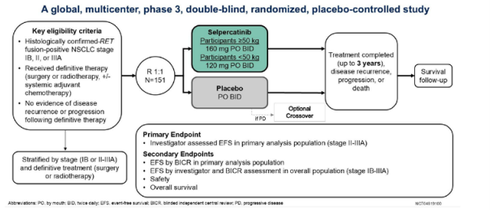


Skoulidis et al., Nat Rev Cancer. 2019

1

LIBRETTO-432: adjuvant Selpercatinib

Early stage NSCLC RET+ (~2% adeno)

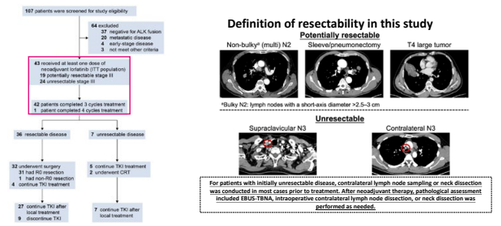


Goldman et al., ASCO 2026

2

LORIN (phase II): Neoadjuvant Lorlatinib

Stage III NSCLC ALK fusions (~5% adeno)

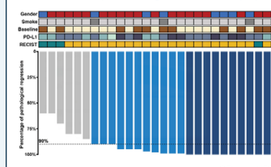


Zhang et al., ASCO 2026

9

LORIN (Neoadj Lorlatinib): pCR (surgery)

Stage III NSCLC ALK fusions (~5% adeno)



Overall	N=32 (n, %)
pCR	15 (47)
MPR	26 (81)
Median/Mean RVT	1%/7%

In NeoADAURA (classic EGFR+):
pCR rate: 9% (osi) / 4% (osi + CT)
MPR: 25% (osi) / 26% (osi+CT)
He et al, JCO 2025

Among patients who underwent surgery, the pCR and MPR rates were **46.9% (15/32) (95%CI, 29.1%-65.2%) [34.9% for ITT]** and **81.3% (26/32) [60.5% for ITT]**, respectively, reaching the primary endpoint.

PR, partial response; SD, stable disease; pCR, pathological complete response; MPR, major pathological response; NA, not assessed; Neg, negative; RVT, residual viable tumor

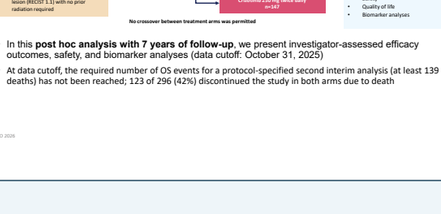
Zhang et al., ASCO 2026

Conversion surgery rate: 75.0%

10

LIBRETTO-432 (adj Selpercatinib): EFS

Early stage NSCLC RET+



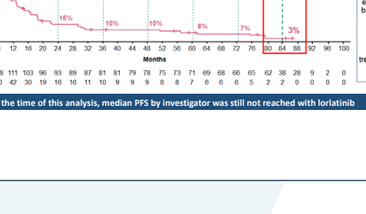
The primary endpoint was met, as selpercatinib demonstrated a statistically significant improvement in EFS

Goldman et al., ASCO 2026

3

LIBRETTO-432 (adj Selpercatinib): EFS

Early stage NSCLC RET+

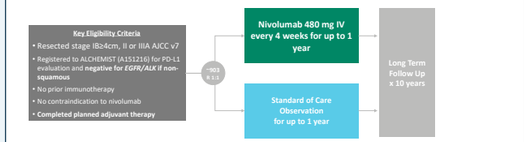


Goldman et al., ASCO 2026

4

ALCHEMIST: adjuvant Nivolumab

Early stage NSCLC without AGAs

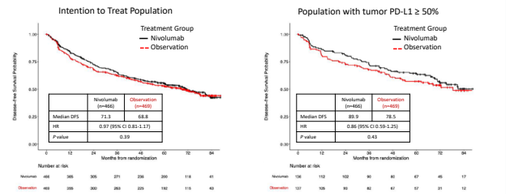


Chaft et al., ASCO 2026

11

ALCHEMIST (adj Nivo): DFS

Early stage NSCLC without AGAs

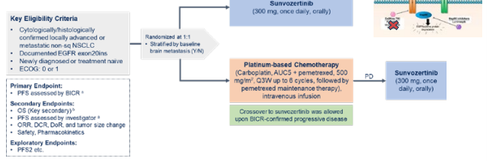


Chaft et al., ASCO 2026

12

WU-KONG28: 1L Sunvozertinib

Metastatic NSCLC EGFR ex20 ins (~2% adeno)

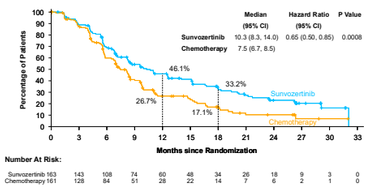


Heymach et al., ASCO 2026

5

WU-KONG28 (1L Sunvozertinib): BICR PFS

Metastatic NSCLC EGFR exon 20 ins



ORR: 59% vs 31% (OR 3.2; 95% CI 2.0, 5.0; P<0.0001)

Median follow-up time: 24.0 months in the sunvozertinib arm and 18.0 months in the chemotherapy arm.

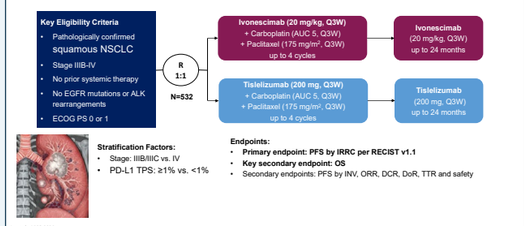
Goldman et al., ASCO 2026

6

HARMONi-6: ivonescimab + CT

VEGF PD-1

1L met NSCLC without AGAs



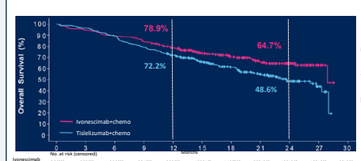
Lu et al., ASCO 2026

13

HARMONi-6 (ivo + CT): OS

VEGF PD-1

1L met NSCLC without AGAs



	Ivonescimab + chemo (N=266)	Tislelizumab + chemo (N=266)
mOS, months (95% CI)	27.89 (27.89, NE)	23.69 (20.11, NE)
Stratified HR (95% CI)	0.66 (0.50, 0.87)	
p-value	0.0017	

- OS significance boundary: 0.0049
- The median OS in the ivonescimab group would have not been reached without the last single event

Abbreviation: mOS, median overall survival; NE, not estimable; HR, hazard ratio; CI, confidence interval

- Data cutoff date: Feb 27, 2026
- Median Follow-up: 21.36 months

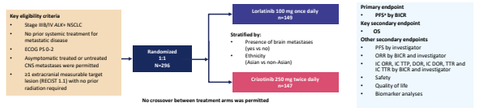
First regimen showing a survival superiority vs chemotherapy + anti-PD-(L)1

Lu et al., ASCO 2026

14

CROWN: 1L Lorlatinib

Metastatic NSCLC ALK fusions (~5% adeno)



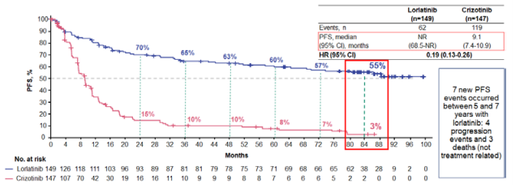
- In this **post hoc analysis with 7 years of follow-up**, we present investigator-assessed efficacy outcomes, safety, and biomarker analyses (data cutoff: October 31, 2025)
- At data cutoff, the required number of OS events for a protocol-specified second interim analysis (at least 139 deaths) has not been reached; 123 of 296 (42%) discontinued the study in both arms due to death

Mok et al., ASCO 2026

7

CROWN (1L Lorlatinib): 7y PFS

Metastatic NSCLC ALK fusions (~5% adeno)

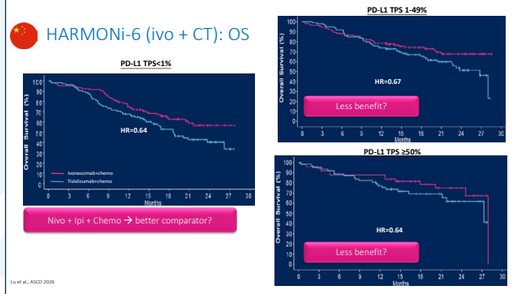


At the time of this analysis, median PFS by investigator was still not reached with lorlatinib

Mok et al., ASCO 2026

8

HARMONi-6 (ivo + CT): OS

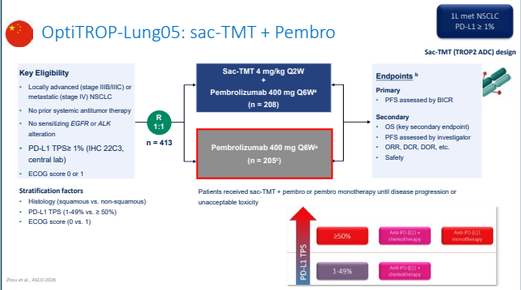


Lu et al., ASCO 2026

15

OptiTROP-Lung05: sac-TMT + Pembro

1L met NSCLC PD-L1 ≥ 1%



Zhou et al., ASCO 2026

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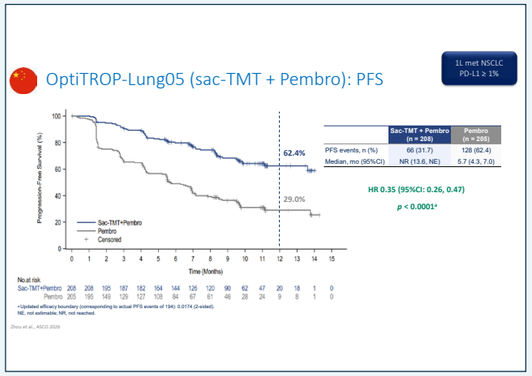

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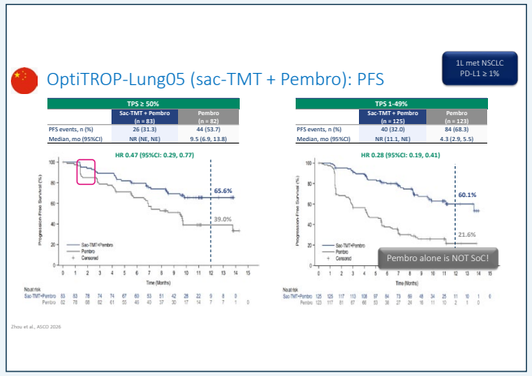

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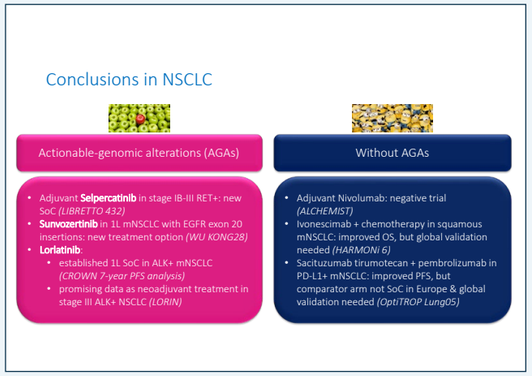

19

RENAL CANCER

Sylvie Rottey, UZ Gent

ctDNA analysis in participants with renal cell carcinoma treated with adjuvant pembrolizumab or placebo in the KEYNOTE-564 trial.
Abstract 4502
Toni K. Choueiri et al.
While sensitivity was low, ctDNA positivity was associated with worse DFS outcomes irrespective of the ctDNA assay used. ctDNA clearance was higher in the pembro arm than in the pbo arm. These data highlight the limitations of these assays in ccRCC.

Durvalumab monotherapy versus active monitoring for resected primary renal cell carcinoma in RAMPART: An international, phase 3, randomized controlled trial.
Abstract LBA4511
James M.G. Larkin et al.
In RAMPART, durvalumab plus tremelimumab was associated with a statistically significant improvement in DFS, which was nog observed with durvalumab monotherapy.

Extended follow-up (6 years) of the phase 2 LITESPARK-004 study of belzutifan in participants with von Hippel-Lindau disease–associated neoplasms.
Abstract 4550
Srinivasan et al.
After 6 years of FU, Belzutifan continues to show durable antitumor activity and a manageable safety profile in pts with VHL associated RCC, CNS HB, pNETs who do not require immediate surgery.

Urinary Bladder Cancer

Enfortumab vedotin plus pembrolizumab (EV+P) vs chemotherapy for previously untreated locally advanced or metastatic urothelial carcinoma (la/mUC): 3.5-year follow-up and response analyses from the phase 3 EV-302 study.
Abstract 4507
Thomas Powles, MD, PhD, et al.
EV 302 represents the longest FU available for EV+P in a phase 3 trial. 3.5 years of median FU, EV+P continues to demonstrate superior efficacy vs chemo, with no safety signals. 2/3 of patients achieving CR converted from an initial PR.

Health-related quality of life (HRQOL) with pembrolizumab or observation for high-risk muscle-invasive urothelial carcinoma after surgery: Results from the AMBASSADOR randomized trial (Alliance A031501).
Abstract 4513
Ronald C. Chen, et al.
Adjuvant pembrolizumab after radical surgery for patients with high risk muscle invasive urothelial carcinoma improved disease free survival without negatively affecting HRQOL.

Health-related quality of life (HRQoL) with neoadjuvant and adjuvant (neoadj-adj) enfortumab vedotin (EV) plus pembrolizumab (pembro) in participants (pts) with muscle-invasive bladder cancer (MIBC) who are cisplatin ineligible: Phase 3 KEYNOTE-905 study. EV 303
Abstract 4510
Peter H. O'Donnell, et al.
The addition of neoadjuvnat EV plus pembro did not decrease HRQoL 18 weeks post surgery relative to RC + PLND alone. BCI bowel and sexual domains worsened in both arms consistent with prior reports of RC impact. Support the use for pts with MIBC ineligible for or declining cis.

Prostate Cancer

TALAPRO-3: Talazoparib (TALA) + enzalutamide (ENZA) compared with placebo (PBO) + ENZA for the treatment of patients (pts) with metastatic castration-sensitive prostate cancer (mCSPC) harboring homologous recombination repair (HRR) gene alterations.
Abstract LBA5007
Neeraj Agarwal, MD, et al.
Treatment with TALA plus ENZA led to statistically significant and clinically meaningful improvement in the primary endpoint of rPFS with a trend towards improved OS vs SOC ENZA in pts with HRRdeficient mCSPC. The safety was manageable and consistent with prior data.

PARP-inhibitoren bij mHSPC — Overzicht Klinische Trials

Fase II/III trials | Stand van zaken juni 2026

Trial	PARPi	Combinatie	Populatie	Biomarker-selectie	Status	rPFS HR	rPFS resultaat	OS	NCT
AMPLITUDE	Niraparib	Abirateron + prednison + ADT	696 pts, HRRm- en HRRm+	HRR-gemuteerd (BRCA2-goedkeuring)	✅ FDA-goedgekeurd dec. 2023 (BRCA2)	0.52 (BRCA) 0.63 (HRR tot.)	BRCA: mPFS vs. 26 mnd (HR 0.52; p<0.0001) HRR totaal: mPFS vs. 29.5 mnd (HR 0.63; p<0.0001) Non-BRCA2: HR 0.88 (NS)	Immatuur; BRCA2: 22% vs. 34%; sterfgevallen	NCT04497844
TALAPRO-3	Talazoparib	Enzalutamide + ADT	599 pts, HRRm- en HRRm+	HRR-gemuteerd	✅ Positief ASCO 2026 / NEJM	0.48 (HRR tot.)	mPFS vs. 45.8 mnd (HR 0.48; p<0.0001) BRCA1/2: HR 0.37 Non-BRCA HRR: HR 0.57	Immatuur; HR 0.77 (trend)	NCT04821622
EvoPAR-Prostate01	Saruparib (AZD5305) PARP1-selectief	ARPi naar keuze (abi / enza / daro) + ADT	HRR+ n=550 HRR− n=1250 (2 cohorten)	Cohort 1: HRR+ Cohort 2: HRR− (uniek)	🔵 Lopend fase III	—	Nog geen fase III data. Fase I/II (PETRANHA) ORR 82.4% bij mHSPC; PSA-ondetecteerbaar op 52w: 76,7%	—	NCT06120491

Legenda & afkortingen

mHSPC = metastatisch hormoon-sensitief prostaatkanker | HRR = homologe recombinatieherstel | PARPi = PARP-remmer | ARPI = androgeenreceptorpadremmer | rPFS = radiografische progressievrije overleving | mNE = mediaan niet bereikt | NS = niet significant | HR = hazard ratio | OS = overall survival
Kleurcode: blauw = AMPLITUDE (niraparib/abi) | groen = TALAPRO-3 (talazoparib/enza) | geel = EvoPAR-PR01 (saruparib, lopend)

TALAPRO-2 vs. TALAPRO-3: Vergelijkende Overzichtstabel

Talazoparib + enzalutamide bij gevorderd prostaatkanker — fase III trials

	TALAPRO-2	TALAPRO-3
OPZET		
Fase	Fase III	Fase III
Setting	Metastatisch castratieresistent (mCRPC)	Metastatisch castratiesensitief (mCSPC)
Populatie	All-comers + HRR-gedeficiënte cohort	Enkel HRR-gemuteerd (a priori selectie)
Aantal patiënten (N)	~399 (HRR-cohort); ~805 (all-comers)	599
Behandeling	Talazoparib 0.5 mg + enzalutamide 160 mg vs. placebo + enzalutamide	Talazoparib 0.5 mg + enzalutamide 160 mg vs. placebo + enzalutamide + ADT
Primair eindpunt	rPFS (BICR)	rPFS (investigator)
Gerandomiseerd	1:1	1:1
Stratificatie	HRR-status, ECOG PS, botmetastasen	De novo vs. relaps, volume, BRCA vs. non-BRCA HRR

Perioperative (neoadjuvant and adjuvant) apalutamide (APA) + androgen deprivation therapy (ADT) vs placebo (PBO) + ADT with radical prostatectomy (RP) in high-risk localized or locally advanced prostate cancer (HR LPC/LAPC): Final analysis of the PROTEUS phase 3 study.
Abstract LBA1
Mary-Ellen Taplin, MD, et al.
APA + ADT significantly increased the curative success of RP in pts with HR LPC/LAPC with a 10 fold higher odds of pCR/MRD and a clinically meaningfull 20% reduction in risk of distant metastasis or death. Sec endpoints all favored APA+ADT. New standard of care ?
Sylvie Rottey June 2026

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Post-ASCO meeting 20 Jun 2026

Genito-urinary cancer

Sylvie Rottey, MD, PhD
Head of Medical Oncology UZGent
Head of Drug Research Unit Ghent

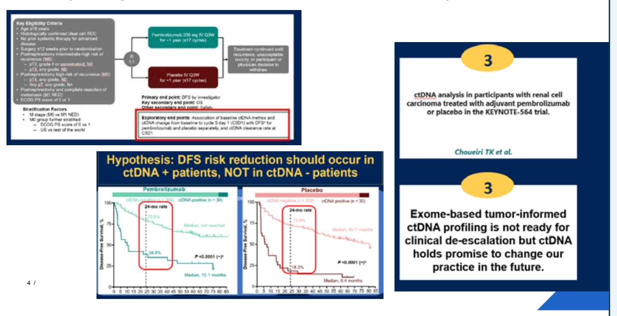
2

Renal Cancer

- Adjuvant CPI :
  - Keynote 564 — *Abstr 4502*
  - Rampart abstr — *LBA4511*
- Belzutifan
  - Litespark 004 – 6 y FU — Abstr4550
  - Litespark 033 ongoing in Belgium

3

Kidney : adjuvant Check Point Inhibition : Keynote 564



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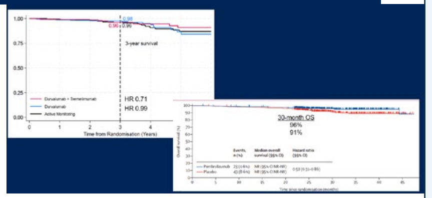
Kidney : adjuvant Check Point Inhibition : RAMPART

Durvalumab monotherapy versus active monitoring for resected primary renal cell carcinoma in RAMPART: An international, investigator-led, phase 3, randomized controlled trial



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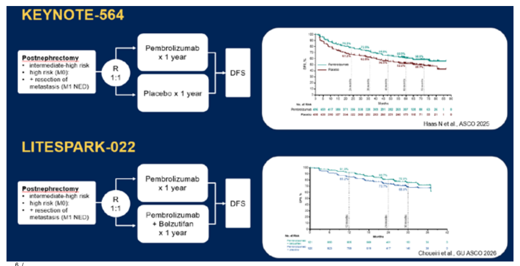
Kidney : adjuvant treatment : what about belzutifan ?



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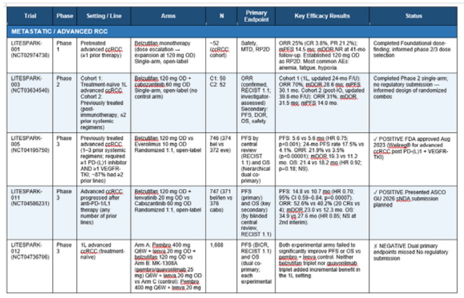
Kidney : what about belzutifan ?



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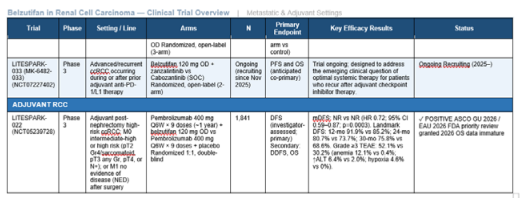


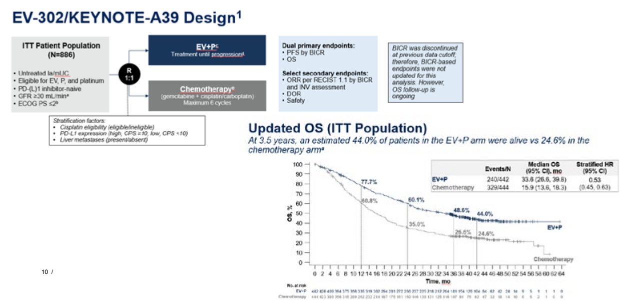
8

Urinary Bladder Cancer

- EV 302 – 3,5 years FU — *Abstr 4507*
- AMBASSADOR — *Abstr 4513*
- Neoadjuvant/adjuvant EV pembro — *Abstr 4510*

9

Bladder : EV 302 study - first line metastatic disease



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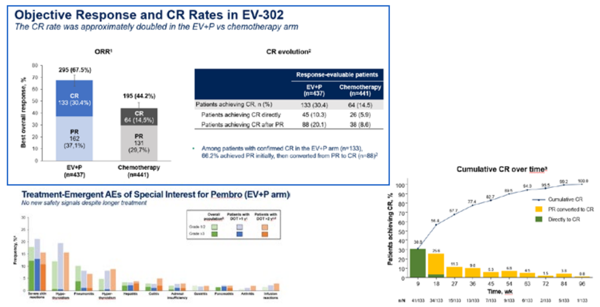
Bladder : EV 302 study - first line metastatic disease



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Bladder : AMBASSADOR- adjuvant pembrolizumab

AMBASSADOR: N=702

- Adjuvant pembrolizumab vs. observation after radical surgery for patients with high-risk muscle-invasive urothelial carcinoma was associated with:
  - Increased fatigue, dyspnea
  - Which modestly affected physical function and ability to perform roles (work, hobbies)
- However, there was no difference in patient assessment of global health or overall HRQOL

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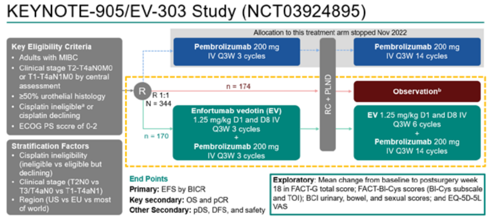
Bladder : peri-operative EV pembro - EV 303

KEYNOTE-905/EV-303 Study (NCT03924895)



13

Bladder : peri-operative EV pembro - EV 303

The addition of perioperative enfortumab vedotin (EV) + pembrolizumab (pembro) to radical cystectomy with standard pelvic lymph node dissection (RC + PLND) was associated with preservation of HRQoL over time relative to RC + PLND alone

Mean changes in general HRQoL, cystectomy-specific HRQoL, and overall health status did not exceed established thresholds for clinically meaningful deterioration

Together with the efficacy and safety results, these PRO findings support the overall benefit–risk profile of perioperative EV + pembro for patients with MIBC who are cisplatin ineligible

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Prostate Cancer

- Peri-operative high risk — *Abstr LBA1*
- PARP inhibition
  - TALAPRO 3 — *Abstr LBA5007*

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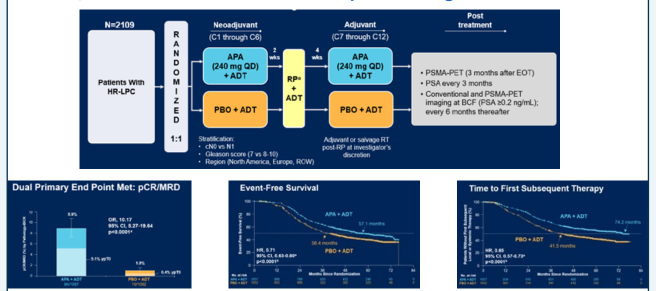
Prostate Cancer : Peri operative high risk PROTEUS



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Prostate Cancer : Peri operative high risk PROTEUS

PROTEUS sets a new standard of care in HR-LPC

Unprecedented Study Design	Enhanced Disease Control of RP	Known Safety Profile	More to Come
• Largest size to date • Novel end points • PSMA-PET inclusion	Significant benefit: • 9× greater pCR/MRD • 20% less risk of MFS • 29% less risk of recurrence or death • 3 years longer time to next treatment	Tolerability of APA+ADT consistent with prior studies	• Substudy comparing with direct RP • Biomarker assessment • Surgical outcomes • Pathology correlates

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Prostate Cancer : PARPi

Trial	PARPi	Combinatie	Populatie	Biomarker-selectie	Status	rPFS HR	rPFS resultaat	OS	NCT
AMPLITUDE	Niraparib	Abirateron + prednison + ADT	696 pts HRRm mHSPC	HRR-gemuteerd (BRCA2-goedkeuring)	✅ FDA-goedgekeurd dec. 2025 (BRCA2)	0,52 (BRCA) 0,63 (HRR tot.)	BRCA: mNR vs. 26 mnd (HR 0,52; p<0,0001) HRR totaal: mNR vs. 29,5 mnd (HR 0,63; p<0,0001) Non-BRCA2: HR 0,88 (NS)	Immatuur; BRCA2: 22% vs. 34% startgevallen	NCT04497844
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18

Prostate Cancer : PARPi TALAPRO – 3

	TALAPRO-2	TALAPRO-3
OPZET		
Fase	Fase III	Fase III
Setting	Metastatisch castratieresistent (mCRPC)	Metastatisch castratiesensitief (mCSPC)
Populatie	All-comers + HRR-gedeficiënte cohort	Enkel HRR-gemuteerd (a priori selectie)
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Primair eindpunt	rPFS (BICR)	rPFS (investigator)
Gerandomiseerd	1:1	1:1
Stratificatie	HRR-status, ECOG PS, botmetastasen	De novo vs. relaps, volume, BRCA vs. non-BRCA HRR

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Prostate Cancer : PARPi TALAPRO – 3

WERKZAAMHEID	
Mediane rPFS — combinatie	Not reached (HRR-cohort)
Mediane rPFS — controle	13,8 maanden (HRR-cohort); 19,5 mnd (all-comers)
Hazard Ratio rPFS (overall)	HR 0,45 (HRR); HR 0,63 (all-comers)
rPFS — BRCA1/2-subgroep	HR 0,20 (80% reductie)
rPFS — non-BRCA HRR	HR 0,68 (32% reductie)
Overall Survival	Significant verbeterd (finale analyse, Lancet 2025)
PSA-responsrate ≥50%	Significant verbeterd vs. controle
VEILIGHEID	
Graad 3–4 TEAE	~46% (HRR-cohort)

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Prostate Cancer : PARPi TALAPRO – 3

	TALAPRO-2	TALAPRO-3
Graad 3–4 TEAE	~46% (HRR-cohort)	79% vs. 41% (controle) CAVE TOX
Anemie (alle graden)	Meest frequent (voornaamste G3/4 TEAE)	71% vs. 22% CAVE TOX
Neutropenie (G3/4)	19% vs. 1%	Frequent (zie profiel)
Permanente stop wegens anemie	Beperkt	5%
MDS / AML	Zelden gerapporteerd	MDS: 3 vs. 1; AML: 2 vs. 0
QoL (PRO)	Geen klinisch relevante achteruitgang	Geen relevante achteruitgang; meer eetlusverlies
STATUS & KLINISCHE IMPLICATIES		
Regulatoire status	FDA-goedkeuring (mCRPC + HRR-alteraties)	Data gepresenteerd ASCO 2026; gepubliceerd in NEJM
Klinische betekenis	Standaard eerstelijnsoptie bij mCRPC met HRR-mutatie	Potentieel nieuwe standaard bij mCSPC met HRR-mutatie
Publicatie	Lancet 2023 (primair); Lancet 2025 (finale OS)	NEJM 2026 (DOI: 10.1056/NEJMoa2604126)

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Post-ASCO meeting 20 Jun 2026

Genito-urinary cancer

Sylvie Rottey, MD, PhD
Head of Medical Oncology UZGent
Head of Drug Research Unit Ghent

UZ GENT · UNIVERSITEIT GENT

BMUC · BSMO ONCOLOGY

Year in review 26 Nov 26 !!

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GYNECOLOGIC CANCER

Jean Francois Baurain, UC Louvain.

POST ASCO MEETING EDUCATION BELGIUM

News from ASCO in Gyneco-Oncology ?

UCLouvain Université · INSTITUT ROI ALBERT II CANCÉROLOGIE ET HÉMATOLOGIE

Prof J-Fr. BAURAIN

29th POST-ASCO La Hulpe 22 June 2024

1

Conflict of Interest

Payments to my institution for consulting, advisory roles or lectures for AstraZeneca, Bristol-Myers Squibb, Esai, Immunocore, GSK, Merck, MSD, Novartis, Pfizer, Pierre-Fabre, Regeneron, Sanofi, Sun Pharma

Taycan, Porsche

Mustang Mach-E, Ford

e-tron GT, Audi

Mustang Cobra, Ford

Vertigo, Gillet

GT 40, Ford

Inscription at ASCO 2026 meeting was partially paid by MSD

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Take-Home Messages from ASCO 2026

The Chicago Theater

CERVICAL CANCER
New ADC targeting TROP2 or Nectin-4

ENDOMETRIAL CANCER
4-Year OS data from NRG-GY018 and RUBY
New ADC targeting FRa or B7-H4
Abemaciclib + Hormonotherapy as an option

OVARIAN CANCER
Novel Immunotherapies are effective
New ADC targeting NaPi2b or c-MET
Timing of cytoreductive surgery isn't important

PRACTICE CHANGING

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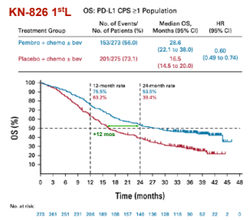
3

Treatment of Recurrent or Metastatic Cervical Cancer

KN-826 1stL OS: PD-L1 CPS ≥1 Population

Treatment Group	No. of Events/ No. of Patients (%)	Median OS, Months (95% CI)	HR (95% CI)
Pembro + chemo ± bev	153/273 (56.0)	28.6 (22.1 to 36.0)	0.60 (0.49 to 0.74)
Placebo + chemo ± bev	201/275 (73.1)	16.5 (14.5 to 20.0)	



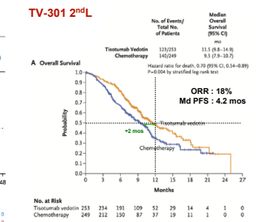
No. at risk:
273 261 251 231 206 185 156 157 140 136 128 116 90 53 22 7 0
275 241 230 207 173 148 129 117 107 91 81 68 45 24 3 0 0

TV-301 2ndL

	No. of Events/ Total No. of Patients	Median Overall Survival (95% CI)
		mo
Tisotumab Vedotin	123/253	11.1 (9.8–14.9)
Chemotherapy	142/249	9.5 (8.3–10.7)

Hazard ratio for death, 0.70 (95% CI, 0.54–0.89)
P=0.004 by stratified log-rank test

A Overall Survival



No. at Risk
Tisotumab vedotin 253 234 191 109 52 29 14 4 1 0
Chemotherapy 249 212 150 87 37 19 11 1 0 0

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Monk BJ, JCO 2023; Vergote I, NEJM 2024

4

Since half of our patients die within two years, where is the wave of ADCs ?

Katsushika HOKUSAI

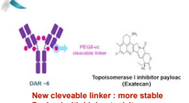
#5507 TROP2 — BAT8008

#5508 Nectin-4 — CRB-701

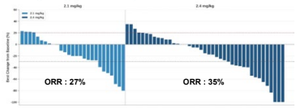
UCLouvain · SONG E, #5507, LORIOT Y, #5508 at ASCO2026 · Huni

5

New Chinese ADC Platform targeting TROP2 beyond 1st Line R/MCC



New cleveable linker : more stable
Payload with higher toxicity



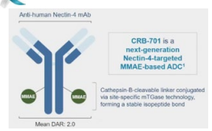
Study design

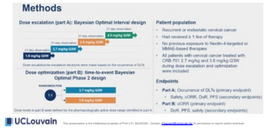
- **Duration of disease control(DoR):** Maximum DoR reached 24m, Overall mDoR was 9.0m.
- **mPFS:** Overall mPFS was 6.7months, with the 2.4 mg/kg dose group achieving a longer mPFS compared to the 2.1 mg/kg group (6.7 vs. 5.4 months).

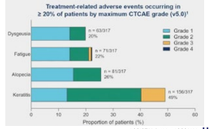
UCLouvain · SONG E, #5507 at ASCO2026 · Huni

6

New ADC Platform targeting Nectin-4 beyond 1st Line R/MCC







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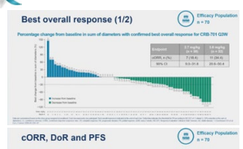
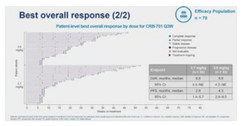
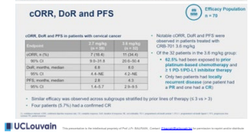
LORIOT Y, #5508 at ASCO2026 Huni

7

New ADC Platform targeting Nectin-4 beyond 1st Line R/MCC







- Notable cORR, DoR and PFS were observed in patients treated with CRB-701 3.6 mg/kg
- Of the 32 patients in the 3.6 mg/kg group:
  - 62.5% had been exposed to prior PD-(L)1 inhibitor therapy and 1 PD-1/PD-L1 inhibitor therapy
  - Only two patients had locally recurrent disease (one patient had a PR and one had a CR)
- Similar efficacy was observed across subgroups stratified by prior lines of therapy (1-3 vs > 3)
- Four patients (5.7%) had a confirmed CR

Still a long road to go !

	TV	BAT8008	CRB-701	CHEMO
Target	TF	TROP2	Nectin-4	
Payload	MMAE	Exatecan	MMAE	
ORR (%)	17.8	29.3	34.4	5.2
md PFS (mos)	4.2	6.7	4.3	2.9
md OS (mos)	11.5	17.8	nr	9.5

Vergote I, NEJM 2024 ; SONG E, #5507; LORIOT Y, #5508 at ASCO2026

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LORIOT Y, #5508 at ASCO2026 Huni

8

Whom really benefits ICI within the pMMR/MSS EC Cohort ?

After ASCO 2026, still an open question !

Post-hoc exploratory analysis in pMMR(PFS)
Serous Histology-*TP53*m

TP53 wt => Selinexor ?

Place of ADC ?

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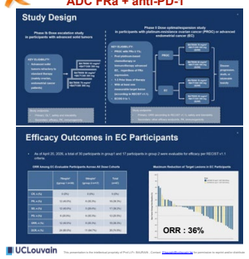
OAKNIN A, ASCO2026 Huni

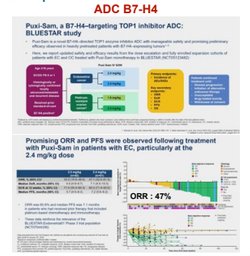
15

New ADC in Endometrial Cancer presented at ASCO

ADC FRa + anti-PD-1



ADC B7-H4



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LONG X, #5512; MILES-WHON L, #5515 at ASCO2026 Huni

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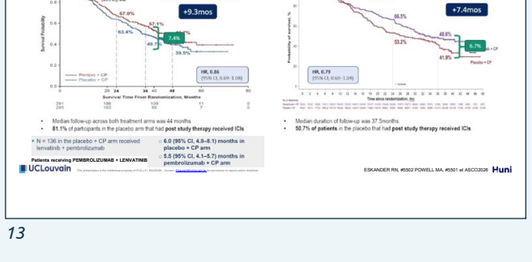
The Cinderella's Story : Major INCREASE in SURVIVAL for EC patients



Carboplatine + Paclitaxel is SOC → **Carboplatine + Paclitaxel + ICI is SOC**

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MILLER DS, JCO 2020; POWELL MA, #5501 at ASCO2026 Huni

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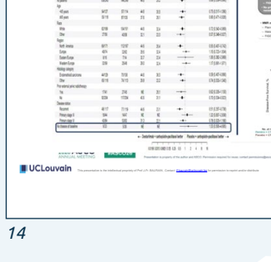
It is even more important for dMMR/MSI EC patients : 4-Year OS

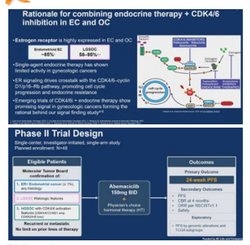


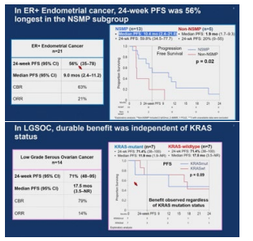
UCLouvain

ESKANDER RN, #5502 POWELL MA, #5501 at ASCO2026 Huni

10

Boosted Hormonotherapy in ER+ EC or LGSOC



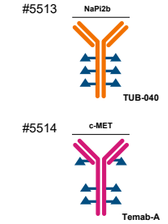


UCLouvain

SILVERSTEIN J, #5510 at ASCO2026 Huni

17

The wave of ADCs for Ovarian Cancer : two new kids in the block

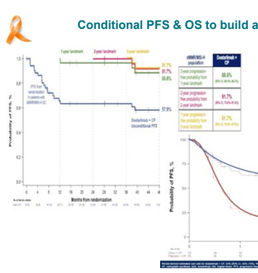


UCLouvain

VAN GORP T, #5513; FLEMING GF, #5508 at ASCO2026 Huni

18

Conditional PFS & OS to build a Cure Model to help Clinicians



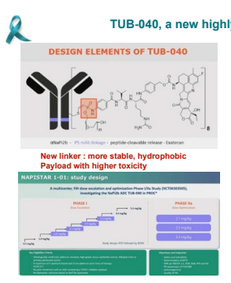
What does it mean ?
If the patient is Progression-free at 2 y, she has more than 90% chance to remains progression-free and alive at 4 y

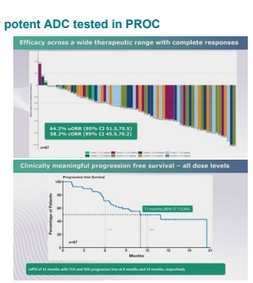
UCLouvain

POWELL MA, #5501 at ASCO2026 Huni

12

TUB-040, a new highly potent ADC tested in PROC





UCLouvain

VAN GORP T, #5513 at ASCO2026 Huni

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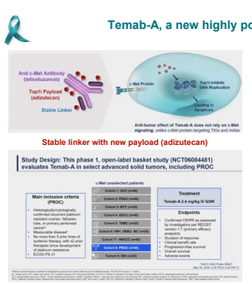
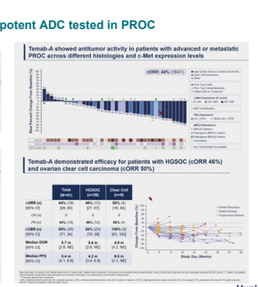
Temab-A, a new highly potent ADC tested in PROC





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FLEMING GF, #5508 at ASCO2026 Huni

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ASCO Update : 4-Year OS for pMMR/MSS EC patients

UCLouvain

ESKANDER RN, #5502 POWELL MA, #5501 at ASCO2026 Huni

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Whom really benefits ICI within the pMMR/MSS EC Cohort ?

Does the presence of disease predict clinical benefit? YES

UCLouvain

OAKNIN A, ASCO2026 Huni

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New forms of Immunotherapies tested in Ovarian Cancer Patients

#5509 **PRAME-TCR** → **IMA203**

#5510 **Peptide Vaccine** → **OSE2101**

UCLouvain

BUSSE A, #5509; LEARY A, #5510 at ASCO2026 Huni

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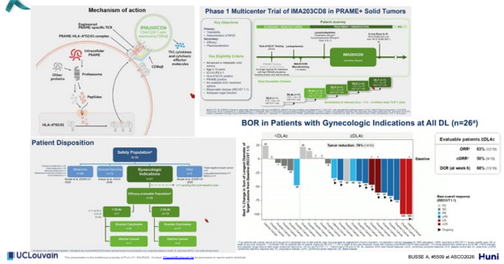
IMA203CD8 is a recombinant PRAME.A2 TCR tested in PROC



UCLouvain

BUSSE A, #5509 at ASCO2026 Huni

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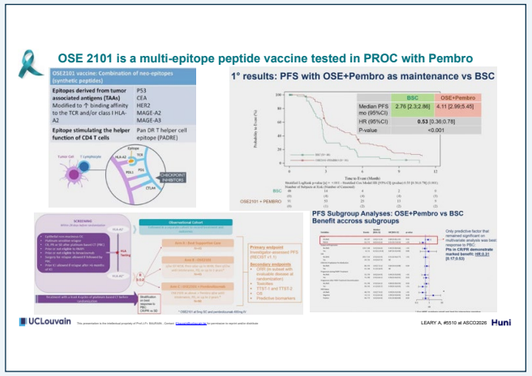

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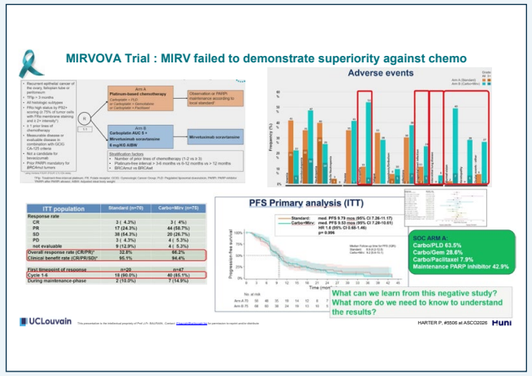

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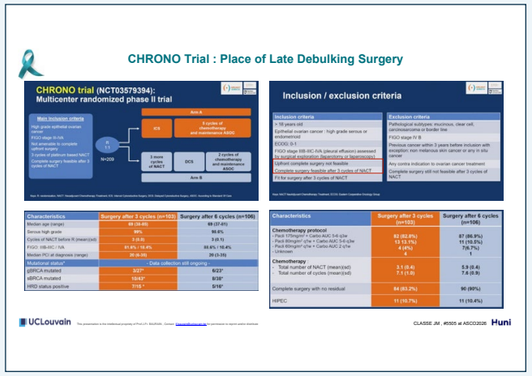

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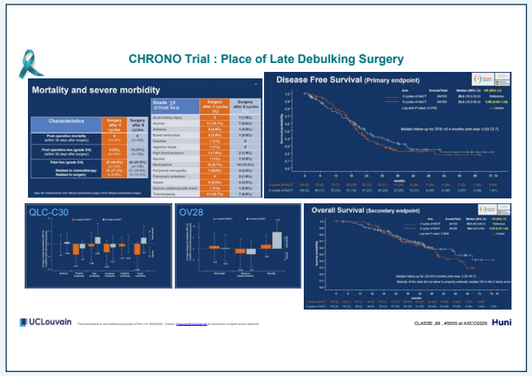

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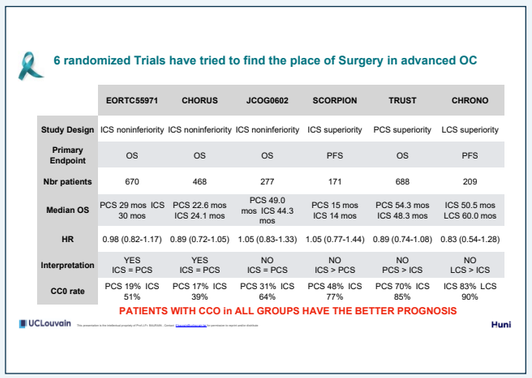

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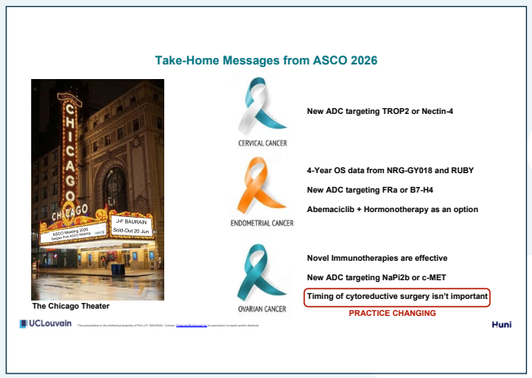

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CLINICIANS GRADE TOXICITY, PATIENTS LIVE IT: HOW CAN WE IMPROVE THE (QUALITY OF) LIFE OF PEOPLE LIVING WITH CANCER BY SUPPORTIVE CARE?

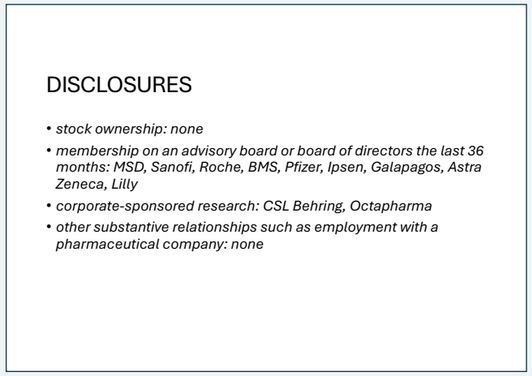
Sandrine Aspeslagh, UZ Brussel

More and more patients with cancer become long survivors, therefore, supportive care during and after cancer specific treatments is essential for patients and their caretakers. Establishing evidence for supportive care is a major challenge since randomized clinical trials, which are the cornerstone of evidence-based cancer care, are very challenging for several reasons. The control arm may not be a perfect control as the fact of participating to a trial studying behavioral changes, such as diet or exercise, in itself, may induce changes in the patients behavior. In addition, many of those trials are often pragmatic in nature and therefore include very heterogeneous populations which in turn make it very challenging to interpret from a statistical point of view.

Several supportive care options such as exercise, diet, digital health applications and yoga were subject of randomized trials presented at ASCO 2026. The YOGAS trial demonstrated that a 4-week yoga intervention in cancer survivors improves mood disturbances and fatigue thereby improving insomnia problems. The follow up of the CHALLENGE trial showed health economic superiority of structured exercise programs for colon cancer survivors. The results of the DeDiCa study, which studied a combination of Mediterranean diet, an exercise program and Vit D supplementation, in non-metastatic breast cancer survivors, suggested that high adherence to the exercise program was related to less breast cancer relapses. The BWEL trial is a telephone-based weight loss intervention which led to significant improvements in physical function and other quality of life outcomes in patients with breast cancer and overweight/obesity. Trials on digital health applications (EMPOWER, EC2C, SUPPORT+) demonstrate that accompanying patients in their day-to-day life may improve of several aspects of quality of life. Especially digital natives such as the AYA (adolescents and young adults) population may be the ideal target group for those digital health applications.

Another part of supportive care concerns adequate care of side effects of cancer therapeuticals. Interventions from dermatologists, ophthalmologists and other organ specialists at ASCO 2026 show that multidisciplinary collaborations lead to better understanding of the organ specific side effects as well as better treatment options (e.g. extracorporeal photopheresis) thereby emphasizing the need for multidisciplinary collaborations. Pneumonitis related to immune checkpoint inhibition (ICI) is often lethal if there is no response to steroids. Rapid response to a combination of a JAK -inhibitor combined with steroids may therefore be of interest in the setting of severe pneumonitis. Beside medical treatments for side effects, exercise may also constitute a cornerstone for a better tolerance as was shown in the URCC 19075 randomized phase II trial for chemotherapy induced neuropathy (CIP). Analysis of vit D status in the SWOG S1714 study showed that vit D deficiency was associated with more CIP, thereby once again suggesting the importance of a correct vit D status in patients with cancer.

1



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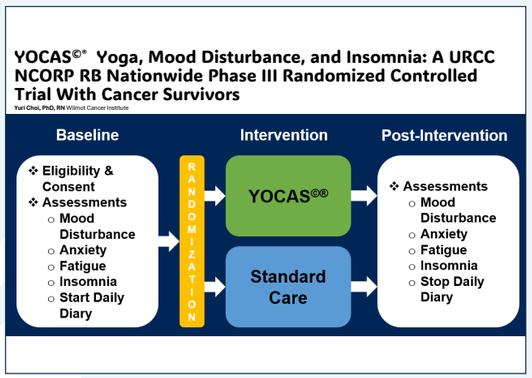

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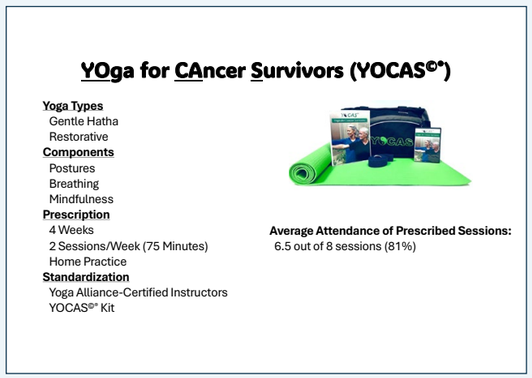

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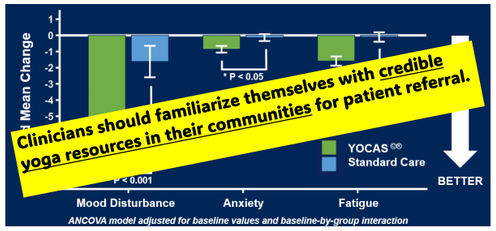
YOCAS℠ Improves Mood Disturbance, Anxiety, and Fatigue



Clinicians should familiarize themselves with credible yoga resources in their communities for patient referral.

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2026 ASCO ANNUAL MEETING

Structured exercise program following adjuvant chemotherapy for colon cancer: A cost-utility analysis of the CHALLENGE trial

Presenter: Kelvin KW Chan, MD PhD

Sunnybrook Odette Cancer Centre, University of Toronto

Canadian Cancer Trials Group

on behalf of: R. Chu, M. Cheung, K. Courneya, C. O'Callaghan, J. Vardy, S. Gill, C. Friedenreich, R. Wong, H. Dhillon, V. Coyle, N. Chua, D. Jonker, R. Meyer, S. Ahmed, J. Zalcberg, S. Clarke, P. O'Brien, P. Tang, R. Wong, H. Lim, M. Burge, M. Brundage, A. Hay, D. Tu, C. Booth and CCTG CO21 the CHALLENGE Trial Investigators & CCTG Committee on Economic Analysis

2026 ASCO ANNUAL MEETING #ASCO26 PRESENTED BY: Kelvin KW Chan, MD PhD

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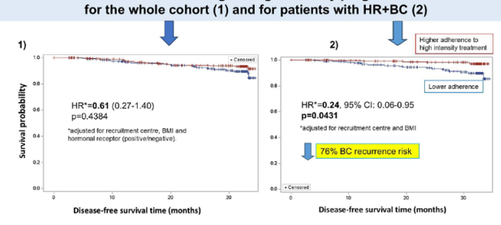
Observational analysis: survival curves by higher vs lower adherence change to high intensity program for the whole cohort (1) and for patients with HR+BC (2)



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2026 ASCO ANNUAL MEETING

Effect of a weight loss intervention (WLI) on quality of life (QOL) and symptoms in women with breast cancer: Results from the Breast Cancer WEight Loss (BWEL) Trial

Jennifer A. Ligibel*, Dawn L. Hershman^, Amylou Dueck, Linda McCall, Brenda Ginos, Pamela J. Goodwin, Anna Weiss, Olwen Hahn, Patricia A. Spears, Electra D. Paskett, Judith O. Hopkins, Erica L. Mayer, Elizabeth Frank, Vanessa Bernstein, Vered Stearns, Julia White, Thomas A. Wadden, Eric P. Winer, Lisa A. Carey, Ann H. Partridge

*co-first author

JENNIFER A. LIGIBEL, MD

Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA

JENNIFER LIGIBEL, MD

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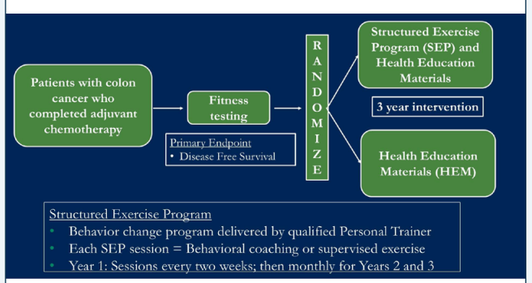

2026 ASCO ANNUAL MEETING #ASCO26 PRESENTED BY: Kelvin KW Chan, MD PhD

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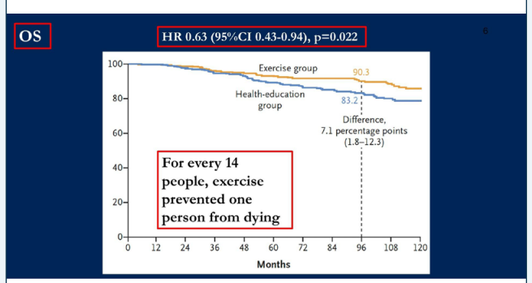

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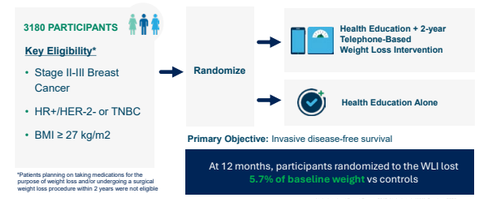
The Breast Cancer Weight Loss Trial



JENNIFER LIGIBEL, MD

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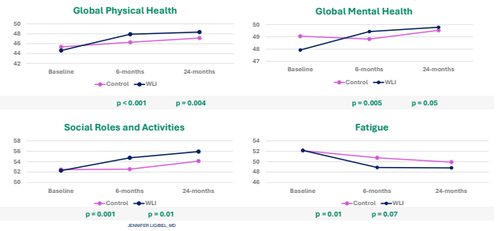
Impact of BWEL WLI on QOL and Symptoms Over Time



JENNIFER LIGIBEL, MD

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Cost of Structured Exercise Program (SEP)

- Total Fixed start-up costs:
  - Based on 8-hour training session and hourly wages as physiotherapist[1]
  - 9 FTE exercise specialists estimated to deliver the SEP to n = 445 participants
- SEP sessions:
  - 1 hour of exercise specialist's time as physiotherapist
  - Mean number of SEP sessions was 63

[1]Government of Canada. Job Bank. Physiotherapist in Canada 2024 [Available from https://www.jobbank.gc.ca/marketreport/wages-occupation/18214/ca]

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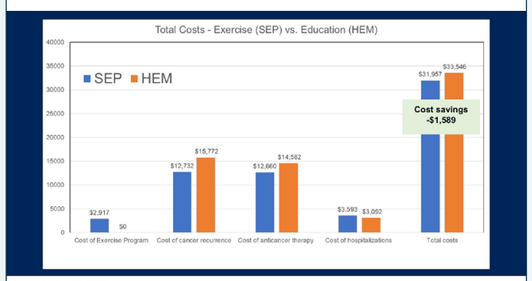

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2026 ASCO ANNUAL MEETING

Let's Get Digital

Reclaiming Quality of Life and Well-Being

Tyler Murphy, MD

Patients do not experience cancer one clinic visit at a time. Increasingly, our supportive care models should not either.

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Key Takeaways

- Digital supportive care can improve meaningful patient outcomes across the cancer continuum.
- The greatest benefits appear in systems combining symptom monitoring with responsive clinical care, of which human connection remains a critical component.
- Reported benefits included improved quality of life, reduced psychological distress, greater self-efficacy, preservation of functional status and reduced hospitalization burden.
- The future challenge is not whether to implement digital supportive care, but rather how to integrate it equitably, sustainably and intelligently.

Tyler Murphy, MD

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2026 ASCO ANNUAL MEETING

The effect of Mediterranean diet, physical activity and vitamin D on breast cancer recurrence and cardiometabolic health: a multicenter randomized trial

Livia S. A. Augustin, PhD, DPH
Epidemiology and Biostatistics Unit,
National Cancer Institute "Fondazione G. Pascale" Napoli (Italy)

2026 ASCO ANNUAL MEETING #ASCO26 PRESENTED BY: Livia S.A. Augustin, PhD, DPH

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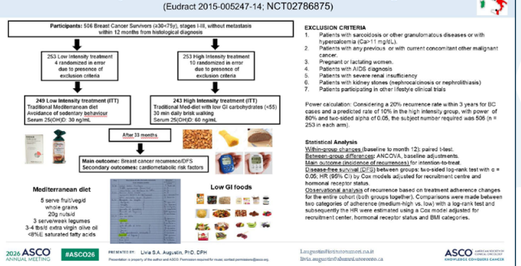
DEDiCa study: multicentric RCT in 7 Italian oncologic centres

(Eudract 2015-005247-14; NCT02786875)



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2026 ASCO ANNUAL MEETING

When does acceptable become unacceptable?

A patient's perspective on toxicities

Sydney Barned, MD

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When Acceptable Becomes Unacceptable

Sydney Barned, MD

20

Why Patients Don't Report

- Fear of dose reductions or treatment loss
- Belief that side effects are a part of treatment
- Uncertainty about what is serious
- Prior dismissal or minimization by healthcare ecosystem
- Desire to not seem difficult or ungrateful

Underreporting is often protective, not careless.

Sydney Barnes, MD

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How We Make It Easier for Patients to Tell the Truth

- Ask about function, not just severity
  - "What has this stopped you from doing?"
  - "What are you pushing through that is becoming unsustainable?"
- Normalize early reporting
  - "Telling us early does not usually mean stopping treatment."
- Create low-friction pathways
  - Clear triage for symptoms, rapid specialist access
- Interdisciplinary toxboards for complex cases

Sydney Barnes, MD

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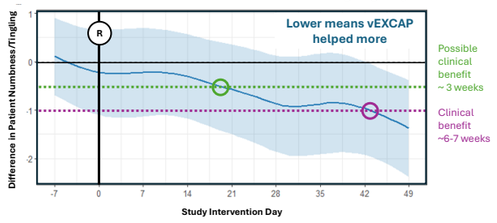
Results: Effects of Exercise on Daily Symptoms



Ian Kleckner

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2026 ASCO ANNUAL MEETING

Vitamin D Insufficiency and Risk of Taxane-Induced Peripheral Neuropathy: Results from SWOG S1714

Nam Nguyen-Hoang, Joseph M Unger, Amy Darke, Michael J Fisch, N Lynn Henry, Dawn L Hershman, Meghna S Trivedi, Daniel L Hertz*

30

2026 ASCO ANNUAL MEETING

The efficacy and safety of add-on ruxolitinib for patients with severe checkpoint inhibitor pneumonitis management with corticosteroids: A multicenter, open-label, randomised phase 2 trial

Yan Xu[1], Xiaoxing Gao[1], Chen Wei[1], Zhimin Zeng[2], Junzhen Gao[3], Xiaoling Yang[4], Xiaoyan Liu[1], Qing Zhou[1], Ruxuan Chen[1], Xiaoyan Si[1], Hanping Wang[1], Jing Zhao[1], Minjiang Chen[1], Wei Zhong[1], Zhiwei Leng[1], Junping Zhang[4], Anwen Liu[2], Hui Huang[1], Mengzhao Wang[1]

[1]Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China; [2]The second affiliated hospital of Nanchang University, Nanchang, China; [3]Affiliated Hospital of Inner Mongolia Medical University, Hohhot, China; [4]Shanxi Bethune Hospital, Shanxi Academy of Medical Sciences, Tongji Shanxi Hospital, Third Hospital of Shanxi Medical University, Taiyuan, China.

Dr. Yan XU

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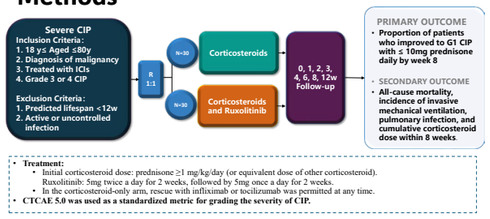
Methods



- **Treatment:**
  - Initial corticosteroid dose: prednisone ≥1 mg/kg/day (or equivalent dose of other corticosteroid). Ruxolitinib: 5mg twice a day for 2 weeks, followed by 5mg once a day for 2 weeks.
  - In the corticosteroid-only arm, rescue with infliximab or tocilizumab was permitted at any time.
- **CTCAE 5.0 was used as a standardized metric for grading the severity of CIP.**

Dr. Yan XU

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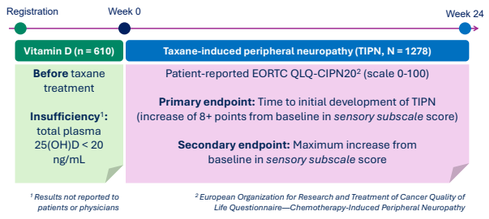
Vitamin D and TIPN measurements



[1] *Results not reported to patients or physicians*

[2] *European Organization for Research and Treatment of Cancer Quality of Life Questionnaire—Chemotherapy-Induced Peripheral Neuropathy*

Nam Nguyen-Hoang, MS

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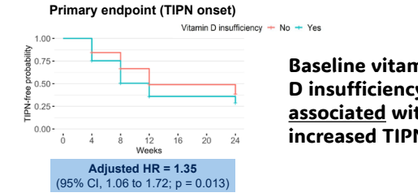
Vitamin D insufficiency is a validated TIPN risk factor



Baseline vitamin D insufficiency is associated with increased TIPN

Nam Nguyen-Hoang, MS

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Efficacy Endpoint

- **At Week 8**
- **G 0-1 CIP:**
  Ruxolitinib group 80.0% (24/30) *vs.*
  Control group 40.0% (12/30)
  (OR, 5.80; 95% CI, 1.67 to 22.93; *p* = 0.003)
- **G 0-1 CIP and ≤10 mg prednisone QD:**
  Ruxolitinib group 66.7% (20/30) *vs.*
  Control group 36.7% (11/30)
  (OR, 3.38; 95% CI, 1.06 to 11.45; *p* = 0.038)

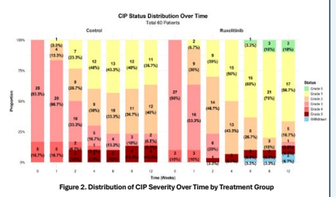

Figure 2. Distribution of CIP Severity Over Time by Treatment Group

Dr. Yan XU

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2026 ASCO ANNUAL MEETING

URCC 19075: A URCC NCORP Research Base nationwide phase II randomized controlled trial (RCT) investigating the effect of exercise on chemotherapy-induced peripheral neurotoxicity (CIPN)

Ian R. Kleckner, Po-Ju Lin, Hongying Sun, Chin-Shang Li, Umang Gada, Dee Murray, Thushini Manuweera, Amber S. Kleckner, Aruna Gowda, Natalya Greyz, Seema Harichand, Arshin Sheybani, Nimish A. Mohile, Bryan Faller, Karen Mustian

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Eligibility: neurotoxic chemo in past 9 months, current symptoms of CIPN, and not currently exercising

BASELINE PRE-INTERVENTION ASSESSMENT (T1)

1.Patient-reported questionnaires (CIPN, Symptoms, Interoception)
2.Tactile Sensitivity Test
3.Start Daily Diary and Pedometer (7 days)
4.Optional – Brain MRI scan

RANDOMIZATION

Arm 1: Exercise: Exercise for Cancer Patients (EXCAP©®) N=66

Wear activity tracker daily

Arm 2: Control: Standard Care / Waitlist N=66

No activity tracker

POST-INTERVENTION ASSESSMENT (T2)

1.Patient-reported questionnaires (CIPN, Symptoms, Interoception)
2.Tactile Sensitivity Test
3.Finish Daily Diary and Pedometer (7 days)
4.Optional – Brain MRI scan

Ian Kleckner

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Virtual Exercise for Cancer Patients (vEXCAP©®)

- Low-moderate intensity home-based walking and resistance exercise intervention
- Virtual 1-hr instruction with 15-min booster meetings at weeks 2 and 4
- Centralized instruction through URCC PEAK Lab

Ian Kleckner

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BREAST CANCER AT ASCO 2026

Earlier intervention, better selection and treatment de-escalation across disease subtypes

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ASCO 2026 highlighted a growing trend toward personalized breast cancer treatment across early and metastatic disease. Beyond new drug development, key studies focused on optimizing how therapies are selected, sequenced, and timed to improve outcomes while reducing overtreatment. Across ER-positive/HER2-negative, triple-negative, and HER2-positive subtypes, data supported earlier intervention in selected patients, biomarker-driven treatment adjustments, and de-escalation strategies in low-risk groups. This summary covers selected ASCO 2026 abstracts and is not exhaustive.

1. ER-positive/HER2-negative Breast Cancer

Early-stage disease: refining chemotherapy de-escalation
In early ER-positive/HER2-negative breast cancer, the phase III OPTIMA trial provided important evidence supporting the use of genomic assays to guide chemotherapy decisions in patients with clinically high-risk disease, including those with node-positive tumors. Among patients with a low Prosigna Risk of Recurrence (ROR) score (≤60), endocrine therapy alone demonstrated non-inferior outcomes compared with chemo-endocrine therapy, with a 5-year invasive breast cancer-free survival of 93.6% versus 94.8% in the control arm (adjusted HR 1.06; 90% CI 0.80–1.40). Crucially, the absence of meaningful chemotherapy benefit was consistent across menopausal status and nodal burden (0 to 9 involved nodes). Importantly, this conclusion now extends to premenopausal women older than 40 years receiving ovarian function suppression, a group previously less well characterized in this context.

Combined with TAILORx, RxPONDER and MINDACT, OPTIMA confirms across more than 18,000 women that gene expression signatures allow safe tailoring of adjuvant chemotherapy in postmenopausal women and in premenopausal women older than 40 years receiving optimal endocrine therapy. These results support broader use of genomic profiling in routine practice.

Metastatic disease: timing becomes the key question
Several phase III studies addressed endocrine resistance from different perspectives. PersevERA evaluated first-line endocrine intensification with giredestrant plus palbociclib but failed to meet its predefined statistical threshold despite a numerical improvement in PFS (33.1 vs 28.2 months; HR 0.89, p = 0.155).

In SERENA-6, patients receiving first-line AI plus CDK4/6 inhibitor underwent serial ctDNA monitoring every 2–3 months; those developing an ESR1 mutation without radiological progression were randomized to switch to camizestrant versus continue AI, both with ongoing CDK4/6 inhibitor. Updated results demonstrated a clinically meaningful PFS benefit (median 16.8 vs 9.2 months; HR 0.45) and improved PFS2 (25.7 vs 19.1 months; HR 0.63), supporting the concept of treating molecular progression before clinical progression. However, important limitations temper the interpretation: the trial simultaneously tests two experimental hypotheses (a new monitoring strategy and a novel drug).

VIKTORIA-1 (study 2) further demonstrated that gedatolisib combined with fulvestrant, with or without palbociclib, approximately doubled progression-free survival compared with alpelisib-based therapy in patients with PIK3CA-mutant HR-positive/HER2-negative advanced disease post-CDK4/6 inhibitor (doublet: ~11.1 vs ~5.6 months; HR 0.51), with better tolerability.

Trial	Regimen	Main message
Early disease		
OPTIMA Phase III adjuvant	*Prosigna ROR-directed CT vs ET*	ET non-inferior to CT in patients with low ROR score (≤60), regardless of nodal burden (0–9 N+) or menopausal status. Gene expression assays now validate chemotherapy de-escalation in women >40 y on OFS. Short follow-up to be considered. *5y iBCFS 93.6% vs 94.8% — HR 1.06; 90% CI 0.80–1.40*
Advanced disease		
SERENA-6 Phase III 1st line	*Camizestrant + CDK4/6i vs AI + CDK4/6i on ESR1 detection*	Switching to camizestrant at molecular (ESR1) progression prolongs PFS and PFS2. OS immature; design conflates monitoring strategy with drug effect. *mPFS 16.8 vs 9.2 m (HR 0.45) · mPFS2 25.7 vs 19.1 m (HR 0.63)*
perseVERA Phase III 1st line	*Giredestrant + palbociclib vs letrozole + palbociclib*	Numerical PFS gain (33.1 vs 28.2 m) did not meet statistical threshold. *HR 0.89; p = 0.155 — primary endpoint not met*
VIKTORIA-1 Phase III 2nd line PIK3CA-mut	*Gedatolisib + fulvestrant ± palbociclib vs alpelisib + fulvestrant*	Multi-target inhibition doubles PFS vs alpelisib with better tolerability in PIK3CA-mutant ABC post-CDK4/6i. FDA approval anticipated mid-2026. *mPFS triplet ~11.1 vs ~5.6 m — HR 0.50* *mPFS doublet 11.3 vs 5.6 months — HR 0.51*

2. Triple-Negative Breast Cancer

Early-stage disease: long-term confirmation and immune priming
The final KEYNOTE-522 analysis (~94-month follow-up) confirmed sustained benefit of pembrolizumab-based neoadjuvant chemo-immunotherapy followed by adjuvant pembrolizumab. At ~8 years, overall survival was 85.1% vs 77.2% with chemotherapy alone (HR 0.64; 95% CI 0.49–0.85), an absolute gain of ~8%. Despite this, a 20–30% risk of recurrence or death persists in node-positive and T3–T4 patients, highlighting the need for further intensification.

The phase II P-RAD trial (TBCRC-053) demonstrated that low-dose preoperative radiotherapy can serve as an immune-priming intervention in node-positive TNBC. Both 9 Gy and 24 Gy combined with pembrolizumab significantly increased tumor T-cell infiltration versus pembrolizumab alone, with the immune response extending to non-irradiated lymph nodes. The 9 Gy dose was sufficient, translating into a 15% higher nodal clearance rate and 10% higher pCR rate.

Metastatic disease: ADCs move to the first line and dissecting TNBC heterogeneity
Three phase III trials reinforced the growing role of ADCs in first-line metastatic TNBC. ASCENT-03 (SG vs chemotherapy, IO-ineligible), ASCENT-04 (SG + pembrolizumab vs chemo + pembrolizumab, PD-L1+), and TROPION-Breast02 (Dato-DXd vs chemotherapy, IO-ineligible) all demonstrated superior progression-free outcomes with ADC-based strategies. TROPION-Breast02 additionally showed an overall survival benefit (dual primary endpoint).

The major new data at ASCO 2026 focused on PFS2. PFS2 is defined as the time from randomization to progression on the next line of therapy or death. Across all three trials, earlier ADC use translated into sustained benefit beyond first progression — median PFS2 improved from 14.0 to 18.2 months in ASCENT-03 (HR 0.70), remained not reached versus 21.0 months in ASCENT-04 (HR 0.67), and improved from 11.8 to 15.6 months in TROPION-Breast02 — despite approximately 80% crossover to SG in the ASCENT control arms. While PFS2 is not validated as a surrogate for OS, the consistency across PFS, PFS2, TFST and TSST is increasingly convincing. The central question in metastatic TNBC is no longer whether ADCs should be used, but how early.

Among the ASCENT trials, biomarker analyses showed benefit across all Trop-2 quartiles, BRCA and HER2 subgroups, with a trend toward greater PFS benefit at higher Trop-2 levels in ASCENT-04.

The FUTURE 2.0 study added a conceptually important finding: in patients with the basal-like immune-suppressed (BLIS) subtype, combining bevacizumab with a Trop-2-targeted ADC achieved response rates exceeding 80% and doubled median PFS versus ADC monotherapy (9.2 vs 4.6 months; HR 0.47). Beyond the numbers, the broader message is compelling: TNBC is not a single disease. Distinct molecular subtypes harbor distinct biological vulnerabilities that can be therapeutically exploited.

Trial	Regimen	Main results
Early disease		
KEYNOTE-522 Phase III (final analysis)	*Pembro + chemo → adj. pembro vs chemo*	8-year OS confirms durable survival benefit. *8y OS 85.1% vs 77.2% — HR 0.64 (95% CI 0.49–0.85)*
P-RAD (TBCRC-053) Phase II Neo-adjuvant	*Preoperative RT (9 or 24 Gy) + pembro + chemo vs pembro + chemo*	Immune SBRT (9 Gy sufficient) converts cold tumors to TCI-high in node+ TNBC, extending the immune response to non-irradiated nodes (+15% ypN0, +10% pCR). *Upper quartile TCI 80% vs 44% — p <0.001*
Advanced disease		
ASCENT-03/04 Phase III 1st line	*04PD-L1+: SG ± pembro vs chemo ± pembro* *03PD-L1-: SG vs chemo*	SG ± pembro new 1L SOC in mTNBC. PFS2 benefit sustained despite ~80% crossover to SG. *PFS2: 18.2 vs 14.0 m (HR 0.70) in 03 · NR vs 21.0 m (HR 0.67) in 04*
TROPION-Breast02 Phase III 1st line IO-ineligible	*Dato-DXd vs chemotherapy (IO-ineligible)*	Overall survival benefit confirmed (dual primary endpoint). *PFS2: 15.6 vs 11.8 m + OS benefit*
FUTURE 2.0 Phase II Platform BLIS subtype	*Trop-2 ADC + bevacizumab vs ADC monotherapy (BLIS subtype)*	Response rates >80% and doubling of PFS with ADC + bevacizumab in the BLIS subtype. *ORR 85% vs 40% · mPFS 9.2 vs 4.6 m (HR 0.47)*

3. HER2-Positive Breast Cancer

Early-stage disease: continuing treatment de-escalation
For patients with stage IA HER2-positive breast cancer, the phase II IRIS-A study explored an intravenous chemotherapy-sparing approach combining oral capecitabine and trastuzumab. After a median follow-up of 66 months, invasive disease-free survival reached 97.8% (95% CI 94.3–99.1) and recurrence-free survival 98.9%, in a predominantly ER-negative (87%), high-grade (55% grade III) population.

Metastatic disease: optimizing HER2-directed sequencing
HER2CLIMB-05 evaluated the addition of tucatinib to standard first-line maintenance with trastuzumab and pertuzumab, after induction chemotherapy (4–8 cycles of THP). In the overall population (n = 654), tucatinib significantly improved median PFS from 16.3 to 24.9 months (HR 0.641; 95% CI 0.514–0.799; p < 0.0001). Benefit was consistent across HR status, de novo vs recurrent disease, and in patients with or without baseline brain metastases, though the absolute improvement was numerically larger in HR-negative disease (12.3 months) than HR-positive (6.9 months). Notably, concurrent endocrine therapy was permitted during maintenance the results highlight the importance of optimized endocrine therapy as part of the maintenance strategy.

Trial	Regimen	Main message
Early disease		
IRIS-A Phase II Adjuvant Stage IA	*Capecitabine + trastuzumab (no IV chemo) — Stage IA*	IV chemo-free adjuvant regimen achieves excellent 5-year outcomes in stage IA HER2+ BC. Single-arm; predominantly T1mic/T1a (80%). *5y iDFS 97.8% · 5y RFS 98.9%*
Advanced disease		
HER2CLIMB-05 Phase III 1st-line maintenance	*Tucatinib + trastuzumab + pertuzumab vs HP maintenance*	Tucatinib added to HP maintenance significantly prolongs PFS. Concurrent ET likely contributes in ER+ patients. Benefit across HR status and BM subgroups. *mPFS 24.9 vs 16.3 m — HR 0.641; p <0.0001*

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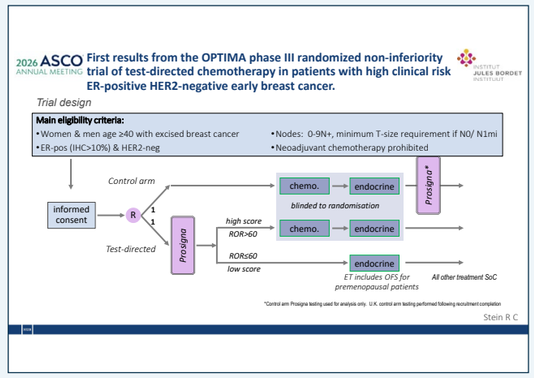

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4. Supportive Care

The phase III REDUSE trial (SAKK 96/12) is the standout result in this category. Denosumab every 12 weeks (after a 4-month monthly induction phase) was non-inferior to the standard every-4-weeks schedule for prevention of symptomatic skeletal events in bone-metastatic breast cancer, with an improved safety profile with lower rates of hypocalcemia and osteonecrosis of the jaw. Denosumab q12w can reduce treatment burden and toxicity without compromising bone protection.

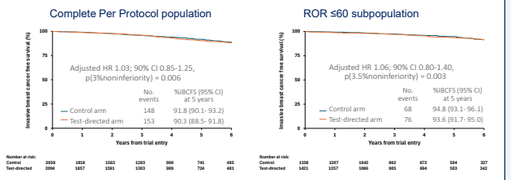
The OASIS trial confirmed that elinzanetant effectively reduces hot flashes regardless of the hormonal therapy being used, providing a non-hormonal option across the full range of adjuvant endocrine regimens.

Trial	Regimen	Main message
REDUSE (SAKK 96/12)	*Denosumab q12w vs q4w (after 4-month loading)*	Denosumab q12w non-inferior to q4w for skeletal event prevention, with lower toxicity (hypocalcemia 30% vs 46%; ONJ 6.9% vs 8.5%). *SSE HR 1.02 (90% CI 0.87–1.20) — non-inferior*
OASIS	*Elinzanetant for hot flashes*	Non-hormonal NK3R antagonist effectively reduces hot flashes across all adjuvant endocrine regimens.

Conclusion
Across breast cancer subtypes, ASCO 2026 highlighted three recurring themes: treatment de-escalation in biologically favorable early-stage disease, earlier intervention in metastatic disease through molecular monitoring or earlier use of highly active therapies, and continued refinement of treatment sequencing. Rather than asking only which drugs are effective, many of the most influential studies focused on a more nuanced question: when should these therapies be introduced to maximize long-term benefit while minimizing unnecessary treatment burden. This shift toward precision in both patient selection and timing may ultimately prove as important as the development of new agents themselves.

Thanks to Luca Arecco, MD, for his help in compiling the data.
Abbreviations: ADC antibody-drug conjugate · AI aromatase inhibitor · BLIS basal-like immune-suppressed · BM brain metastases · CT chemotherapy · ET endocrine therapy · HR hazard ratio · iDFS invasive disease-free survival · IO immunotherapy · mPFS median progression-free survival · OFS ovarian function suppression · pCR pathological complete response · RFS recurrence-free survival · SOC standard of care · SSE symptomatic skeletal event · TCI tumour T-cell infiltration · TFST/TSST time to first/second subsequent therapy

Invasive Breast Cancer Free Survival



Demonstrated non-inferiority limit = 2%
No certainty of chemotherapy benefit
1.5% observed 5-year difference –favors chemotherapy

Demonstrated non-inferiority limit = 2%
No certainty of chemotherapy benefit
1.2% observed 5-year difference –favors chemotherapy

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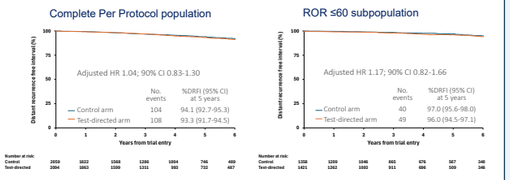
Distant Recurrence Free Interval



0.8% observed 5-year difference –favors chemotherapy

1.0% observed 5-year difference –favors chemotherapy

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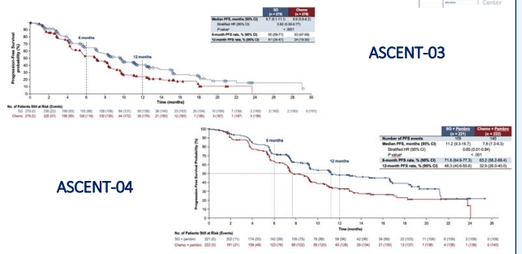
ASCENT-03 and ASCENT-04



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ASCENT-03 and ASCENT-04 comparison

Variable	ASCENT-03 SG vs chemotherapy	ASCENT-04 / KEYNOTE-D19 SG + pembrolizumab vs chemotherapy + pembrolizumab
	PFS2 and subsequent therapies	
PFS2 events	114 vs 143 events.	55 vs 83 events.
Median PFS2	18.2 months (95% CI 15.5-NR) vs 14.0 months (95% CI 12.5-17.4). HR 0.70 (95% CI 0.55-0.90).	NR (95% CI NR-NR) vs 21.0 months (95% CI 16.0-NR). HR 0.67 (95% CI 0.48-0.95).
Interpretation of PFS2	Longer PFS2 with 1L SG despite high crossover to SG in the chemotherapy arm.	Longer PFS2 with 1L SG + pembro despite high crossover to SG in the control arm.
Subsequent SG / crossover	147/179 (82%) participants receiving subsequent therapy received SG in any subsequent line. In 2L, SG was received by 142/179 (79%) in the chemotherapy arm.	96/119 (81%) participants receiving subsequent therapy received SG in any subsequent line. In 2L, SG was received by 92/119 (77%) in the control arm.
Time to first subsequent therapy	11.2 vs 7.9 months; HR 0.61 (95% CI 0.50-0.75).	17.1 vs 9.8 months; HR 0.59 (95% CI 0.46-0.76).
Time to second subsequent therapy	17.3 vs 16.6 months; HR 0.82 (95% CI 0.64-1.05).	NR (95% CI 22.9-NR) vs 21.0 months (95% CI 16.6-NR); HR 0.82 (95% CI 0.59-1.14).
	Biomarker analyses	
Trop-2 expression	PFS longer with SG across all Trop-2 quartiles. NO clear trend of greater efficacy at higher Trop-2 expression.	PFS longer with SG + pembrolizumab across all Trop-2 quartiles. Greater benefit with SG described in Q3/Q4.
BRCA status	Benefit observed regardless of tBRCA status; numerically longer PFS in mutant than WT subgroup, but small numbers.	Benefit direction generally observed across tBRCA subgroups, but mutant subgroup estimate imprecise and sample size small.
HER2	PFS longer with SG across HER2 IHC 0 and HER2-low subgroups.	PFS longer with SG + pembrolizumab across HER2 IHC 0 and HER2-low subgroups.
Biomarker take-home messages	No biomarker subgroup appears to exclude benefit from SG	Benefit of SG + pembrolizumab is consistent across subgroups.

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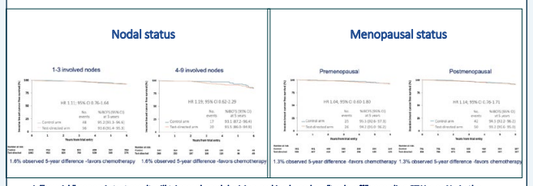
IBCFS in low ROR score population



- A "low risk" genomic test result will trigger shared decision-making based on "trade-off" regarding CT Yes or No in the presence of optimal endocrine therapy (OFS)
- Current knowledge indicates a very low (if any) CT benefit independent of nodal burden and menopausal status
- Some uncertainty remains in view of relatively small key sub populations and short follow-up in the OPTIMA trial

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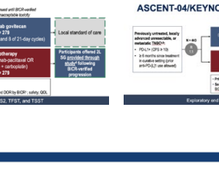
Endocrine therapy (ET)NOT INFERIOR to ET + Chemotherapy in the presence of a favorable multigene expression assay*

N = 18,108 women recruited in 4 academic trials over 25 years

5y iDFS HR = 1.08 (95% CI 0.94 – 1.24)
Absolute difference= 1%

5y iBCFS
Overall HR 1.03 (90% CI 0.85-1.25) for control vs test arm
Absolute difference= 1.5%



5y DMFS for ET alone in High clin/ low gen risk= 95.1% (95% CI 93.1 – 96.6%)

Required:92%

Randomized non inferiority trials (power > 80%)
*Single arm** de-escalation trial
Trial testing an interaction

Node - 1 – 3 N+ 1-9 N + Increasing tumor burden

Non-significant interaction between RS and CTX benefit (p= 0.35)
Overall Sy iDFS (ET ± CTX)
Absolute difference = 1.2%

* ONCOTYPE DX®: Tailor-X RX, ponder
* MammaPrint®: MINDACT
* Prosigna®: Optima

(1) Sparano, NEJM 2018 (2) Piccart, Lancet 2021
(3) Kalinsky, NEJM 2021 (4) Stein, ASCO 2026

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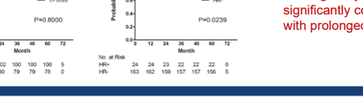
2026 ASCO ANNUAL MEETING — Primary Results from the Triple Negative Cohort of TBCRC-053 (P-RAD): A Randomized Trial of N0, Low, or High Dose Preoperative RADiation with Pembrolizumab and Chemotherapy in Node-Positive Breast Cancer

Can pre-op breast RT serve as an immune-priming intervention to improve response to chemo-immunotherapy?



Outstanding Questions:
1) Does RT+aPD1 achieve greater benefit than aPD1 alone?
2) Is concurrent RT+aPD1 more effective than sequential?
3) What RT dose is optimal for immune activation?

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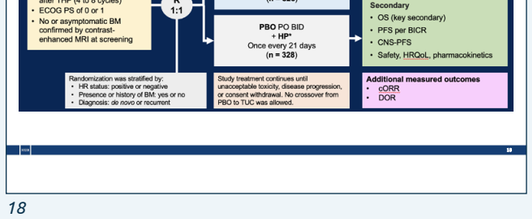
TBCRC-053: P-RAD Multicenter Randomized Phase II Clinical Trial



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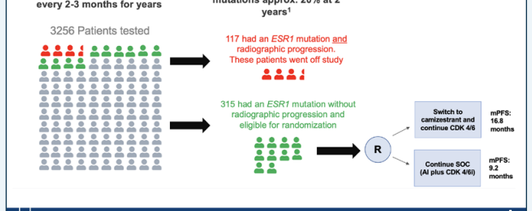
SERENA 6 Consort Diagram (Strategy)



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2026 ASCO ANNUAL MEETING — First-line camizestrant for emergent ESR1 mutations in advanced breast cancer: Final progression-free survival 2 from the Phase III SERENA-6 trial

Phase III, randomized, double-blind, placebo-controlled study (NCT04964934)

- Adult patients with ER+/HER2– ABC
- All patients had received AI + CDK4/6i (palbociclib, ribociclib, or abemaciclib) as initial endocrine-based therapy for ABC for at least 6 months
- *ESR1*m detected in ctDNA with no evidence of disease progression
- ≤1 prior line of chemotherapy for ABC

R 1:1 n=315
Camizestrant (75 mg QD) + continuing CDK4/6i + placebo for AI (n=157)*
Continuing AI + CDK4/6i + placebo for camizestrant (n=158)*
Treatment continued until disease progression, unacceptable toxicity, patient withdrawal, or death

The study was powered for PFS (primary endpoint) and the key secondary endpoint of investigator-assessed PFS2

Randomization — PFS — First PD or death — PFS2[1] — Second PD or death
RECIST v1.1 tumor assessment
Every 8 weeks for 18 months and then every 12 weeks (RECIST mandatory)
Every 8–12 weeks (RECIST recommended)

Bidard F-C

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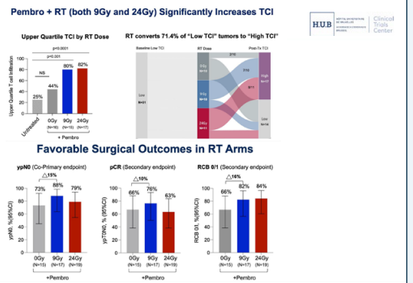
Pembro + RT (both 9Gy and 24Gy) Significantly Increases TCI



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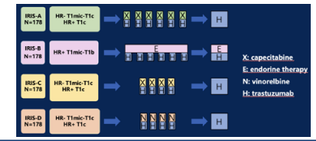
2026 ASCO ANNUAL MEETING — Adjuvant Capecitabine and Trastuzumab for Stage IA HER2 positive Breast Cancer (IRIS-A): A Phase II Clinical Trial

The series of the "IRIS" study are designed as single-group, phase II trials regarding de-escalation of adjuvant therapy without intravenous chemotherapy in early-stage HER2+ BCs.



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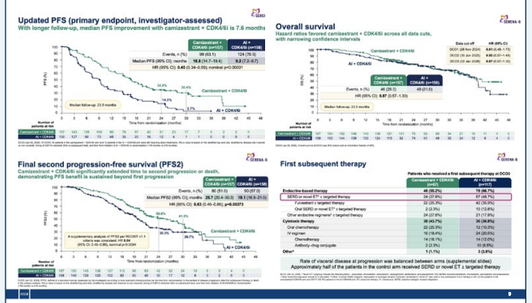

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ASCENT-03 and ASCENT-04 trials

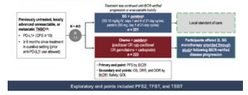
2026 ASCO ANNUAL MEETING

Progression-Free Survival After Next Line of Treatment (PFS2) and Subsequent Therapies in the ASCENT-03 Study of Participants With Previously Untreated Metastatic Triple-Negative Breast Cancer Treated With Sacituzumab Govitecan vs Chemotherapy

ASCENT-03: Study Design

Progression-Free Survival After Next Line of Treatment (PFS2) and Subsequent Therapies in the ASCENT-04 Study of Participants With Previously Untreated PD-L1+ Metastatic Triple-Negative Breast Cancer Treated With Sacituzumab Govitecan Plus Pembrolizumab vs Chemotherapy Plus Pembrolizumab

ASCENT-04/KEYNOTE-D19: Study Design



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The IRIS-A trial

- 5-year iDFS: **97.8%** (95% CI, 94.3 to 99.1)
- 5-year RFS: **98.9%** (95%CI, 95.7 to 99.7)
- HR negativity was significantly correlated with prolonged survival

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2026 ASCO ANNUAL MEETING — HER2CLIMB-05 :Efficacy and safety of tucatinib (TUC) vs placebo (PBO) combined with trastuzumab and pertuzumab (HP) as maintenance therapy for HER2+ metastatic BC by stratified subgroups.

HER2CLIMB-05 is a randomized, double-blind, placebo-controlled, international, phase 3 trial (NCT05132582)

Key Eligibility Criteria
- Centrally confirmed HER2+ MBC
- No evidence of progression after THP (4 to 8 cycles)
- ECOG PS of 0 or 1
- No or asymptomatic BM confirmed by contrast-enhanced MRI at screening

R 1:1

1L Maintenance Therapy
- **TUC** 300 mg PO BID + HP* Once every 21 days (n = 326)
- **PBO** PO BID + HP* Once every 21 days (n = 328)

Randomization was stratified by:
- HR status: positive or negative
- Presence or history of BM: yes or no
- Diagnosis: *de novo* or recurrent

Study treatment continues until unacceptable toxicity, disease progression, or consent withdrawal. No crossover from PBO to TUC was allowed.

Endpoints

Primary
- Investigator-assessed PFS per RECIST v1.1

Secondary
- OS (key secondary)
- PFS per BICR
- CNS-PFS
- Safety, HRQoL, pharmacokinetics

Additional measured outcomes
- cORR
- DOR

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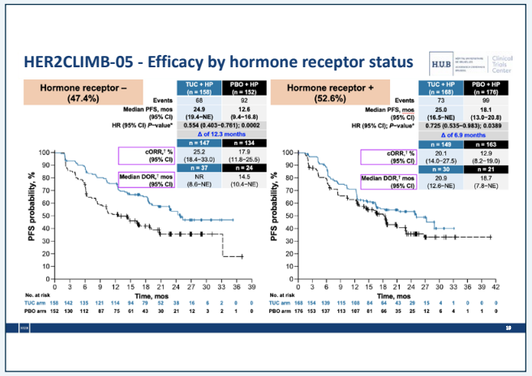

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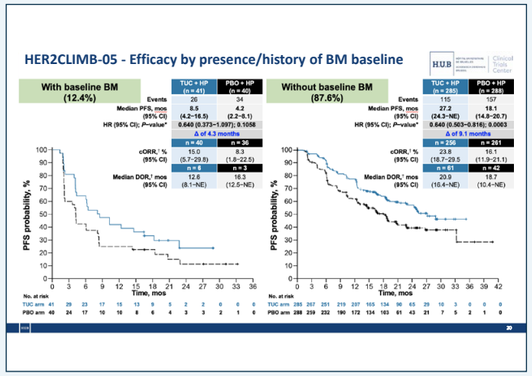

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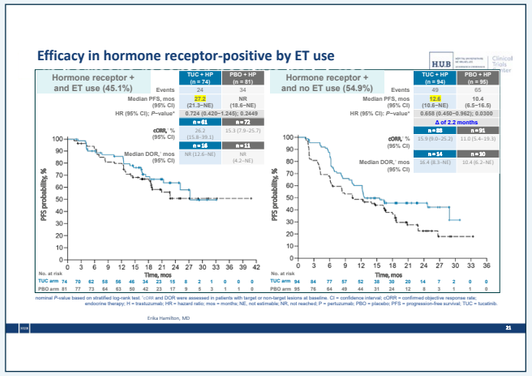

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For 175 years, we have worked to make a difference for all who rely on us.

Every day, we apply our science and our resources to bring therapies to people that can expand and significantly improve their lives.

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Breakthroughs that change patients' lives

Reimagining medicine, together.

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FA-11671433 - 04/05/2026

Responsible editor: Novartis Pharma, NV • Kouterveldstraat 2, bus 0501, 1831 Diegem, Belgium

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NS ID XL-5672-Revision date 10/2025-LB Local code 1971