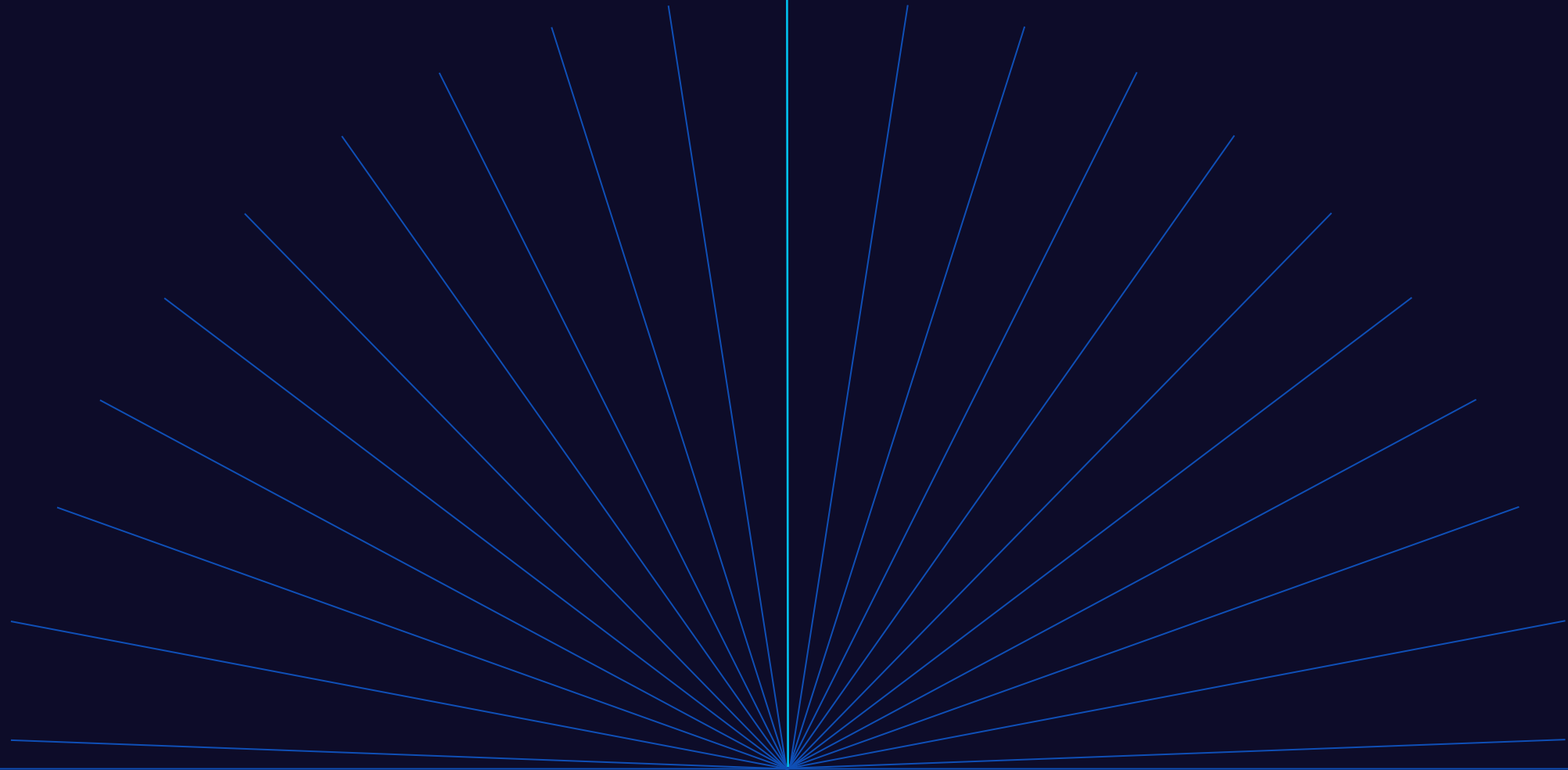




Sleuth

ESMO 2026 Preview

Key takeaways going into ESMO

What the ESMO 2026 program shows before the congress opens

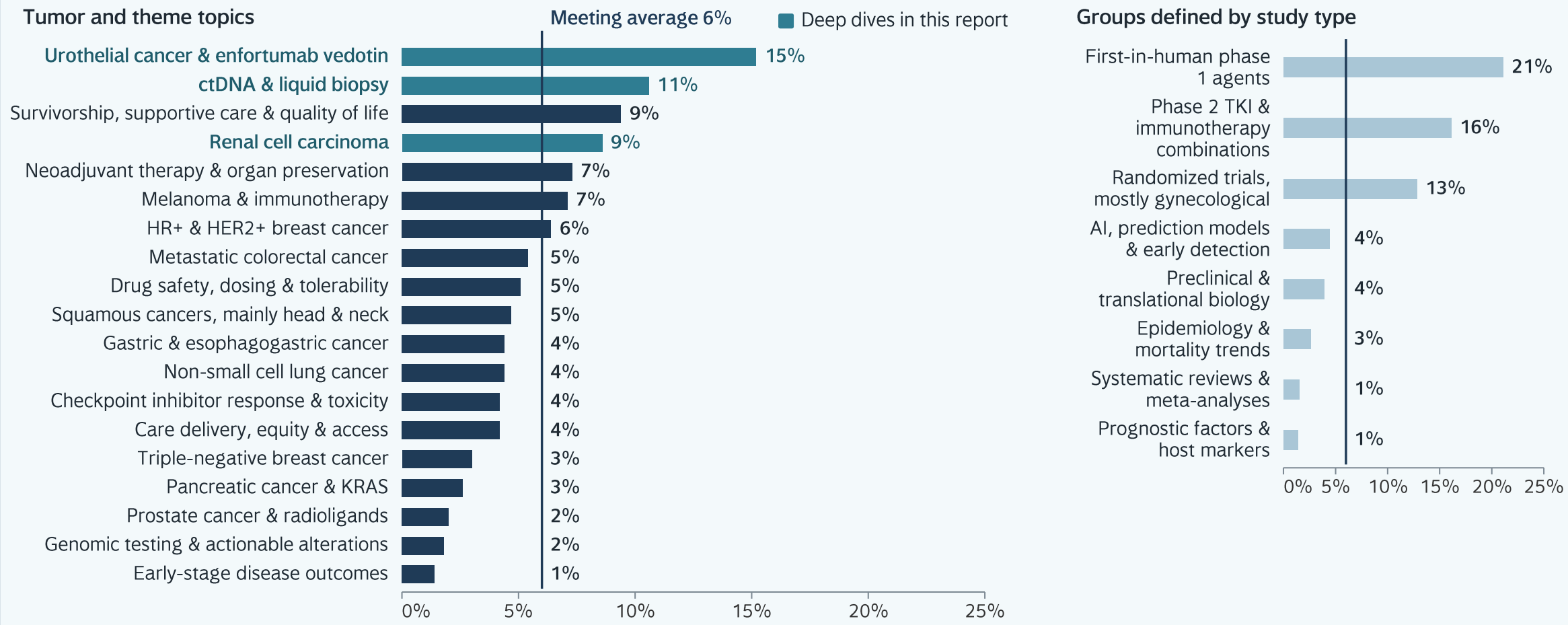
- 1** Urothelial cancer, ctDNA and renal cancer beat the 6% oral average, each with new FDA approvals Page 3
- 2** EV + pembro moved from metastatic to muscle-invasive bladder cancer in 23 months Page 4
- 3** Belzutifan met PFS or DFS in 3 of 4 kidney cancer phase 3s Page 5
- 4** ctDNA is crossing from a prognostic marker into a treatment decision Page 6
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- 7** G12D drugs lead ESMO 2026 KRAS-inhibitor abstracts, mostly in combinations Page 9
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Urothelial cancer, ctDNA and renal cancer beat the 6% average for orals

Oral slots flag what ESMO rates most practice-changing, and these 3 topics win them at 1.4 to 2.5x the average

Share of each topic's ~4.2K abstracts presented orally



EV + pembro moved from metastatic to muscle-invasive bladder cancer in 23 months

MIBC trials now ask which ADC regimen to use and whether cisplatin or the bladder can be dropped

The path to muscle-invasive bladder cancer

EV regimens

- Dec 2023** ● FDA: EV + pembrolizumab, first-line metastatic
- Oct 2025** ● KEYNOTE-905 at ESMO 2025: EV + pembrolizumab, cisplatin-ineligible MIBC, EFS HR 0.40
- Nov 2025** ● FDA: EV + pembrolizumab, cisplatin-ineligible MIBC
- Jul 2026** ● FDA: EV + pembrolizumab, MIBC regardless of cisplatin eligibility (KEYNOTE-B15)
- Oct 2026** ● VOLGA at ESMO 2026: durvalumab + EV, cisplatin-ineligible MIBC

PD-1 + cisplatin

- Oct 2026** ● ESMO 2026: pembrolizumab or nivolumab + cisplatin, no EFS gain (HR 0.88, 0.94)

Key ADC regimens in early urothelial cancer

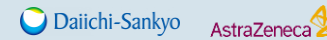
EV + pembrolizumab
Nectin-4 · perioperative
Approved in the U.S.



EV + durvalumab
Nectin-4 · perioperative
Phase 3, positive topline



Datopotamab deruxtecan
TROP2 · after surgery
Phase 3, recruiting



Sacituzumab tirumotecan
TROP2 · bladder-sparing
Phase 3, opening Oct 2026



SHR-A2102
Nectin-4 · perioperative
Phase 2/3



Disitamab vedotin
HER2 · neoadjuvant MIBC and
upper-tract
Phase 2, mostly China



Sacituzumab govitecan
TROP2 · neoadjuvant
Phase 2



9MW2821
Nectin-4 · perioperative
Phase 2



More than a dozen EV trials now target early MIBC or upper-tract cancer, 4 of them phase 3

Sleuth Insight: Sequencing is not static. As EV + pembro moves into early-stage disease, relapsing patients will arrive EV- and PD-1-exposed, which changes which treatments open up in later lines. Upcoming readouts show where those openings will be before the standard moves.

Belzutifan met PFS or DFS in 3 of 4 kidney cancer phase 3s

It blocks HIF-2α, a driver in most clear cell kidney cancers that immunotherapy and TKIs do not reach

Key trials adding belzutifan, by setting and partner

	Monotherapy	+ pembrolizumab	+ lenvatinib	+ cabozantinib	+ zanzalintinib	+ pembrolizumab + lenvatinib
VHL disease	Approved 2021 · phase 2-based	.	.	.	.	.
After surgery	.	Ph3 met DFS · HR 0.72 · approved 2026	.	.	.	.
First line	.	.	.	Phase 2 · ORR 70%	.	Ph3 failed · PFS HR 1.08
After immunotherapy	.	.	Ph3 met PFS · HR 0.74 · approved 2026	Phase 2 · ORR 31%	.	.
Relapse after adjuvant immunotherapy	.	.	.	.	Phase 3 ongoing	.
Later lines	Ph3 met PFS · HR 0.75 · approved 2023	.	.	.	Phase 3 ongoing	.
Beyond kidney	PPGL approved 2025 · phase 2-based	.	.	.	.	GI cancers · phase 2

Unmet need

Metastatic kidney cancer has a 19% 5-year relative survival rate

Combination value

An oral, once-daily HIF-2α blocker whose anemia and low oxygen differ from immune or TKI side effects

Doublet vs triplet

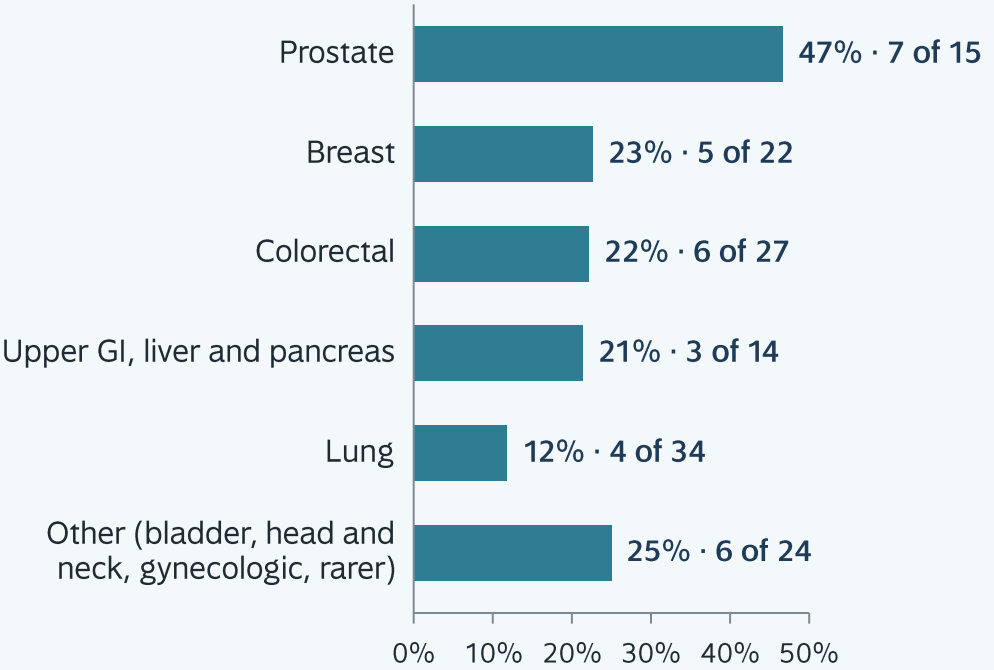
52% stopped a drug for side effects on the first-line triplet vs 36% on pembrolizumab + lenvatinib. The authors suggest this may have limited its effect

Sleuth Insight: In kidney cancer, belzutifan succeeded by itself or as a second drug but failed as a third, and the COSMIC-313 triplet gained no OS. Here, the right doublet has mattered more than a third drug.

ctDNA is crossing from a prognostic marker into a treatment decision

Two 2026 FDA approvals act on ctDNA found after bladder surgery or during breast cancer therapy

Share of ctDNA abstracts inside industry drug trials¹, by tumor (136)



ctDNA uses that change treatment

Use	Status	Evidence
Genotyping in advanced disease	Routine	FDA plasma companion tests in lung, breast, colorectal, prostate
Treat after surgery if ctDNA is found	FDA approved, bladder, May 2026	IMvigor011: DFS HR 0.64, OS HR 0.59
Switch therapy when ESR1 mutation appears	FDA accelerated approval, breast, Sep 2026	SERENA-6: PFS HR 0.44. FDA says more evidence is needed to confirm clinical benefit ²
Drop chemotherapy when ctDNA is negative	Mixed in colon	DYNAMIC: less chemo, RFS held (stage II). DYNAMIC-III: not met (stage III)
Test, then treat, at ESMO 2026	In trials	15 abstracts, 0 randomized efficacy readouts

Sleuth Insight: ctDNA can flag relapse or resistance before scans do, and IMvigor011 and SERENA-6 turned that into treatment changes. Its uses differ by tumor, and adoption is likely to come one disease at a time.



7 of 12 non-metastatic checkpoint phase 3s met their primary endpoint

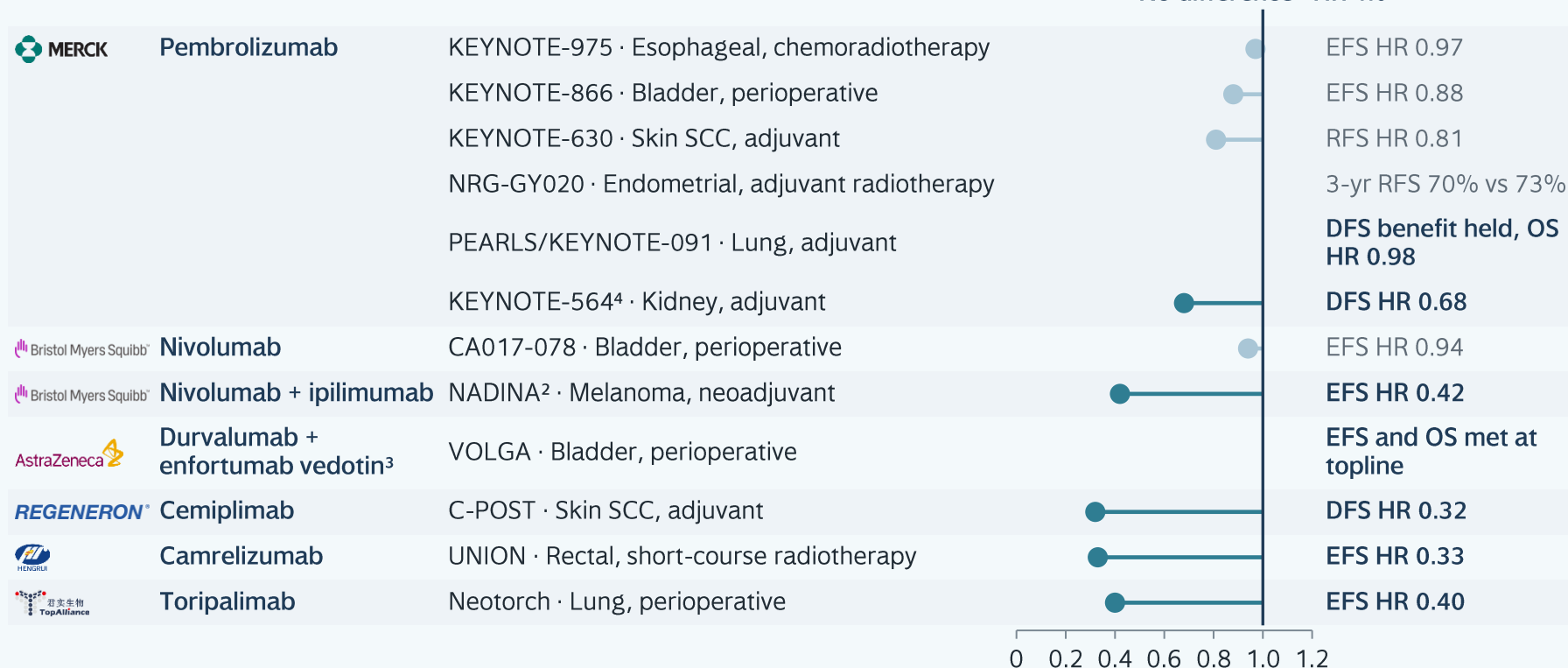
Pembrolizumab met it in 2 of 6 phase 3s, with its U.S. compound patent ending in 2028

Checkpoint phase 3 readouts before metastasis at ESMO 2026, by drug

● Met primary endpoint

● Did not meet primary endpoint

No difference · HR 1.0



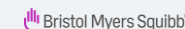
Keytruda



\$31.7B in 2025, ~49% of Merck revenue

U.S. compound patent ends 2028

Opdivo



\$10.3B in 2025, 21% of BMS revenue

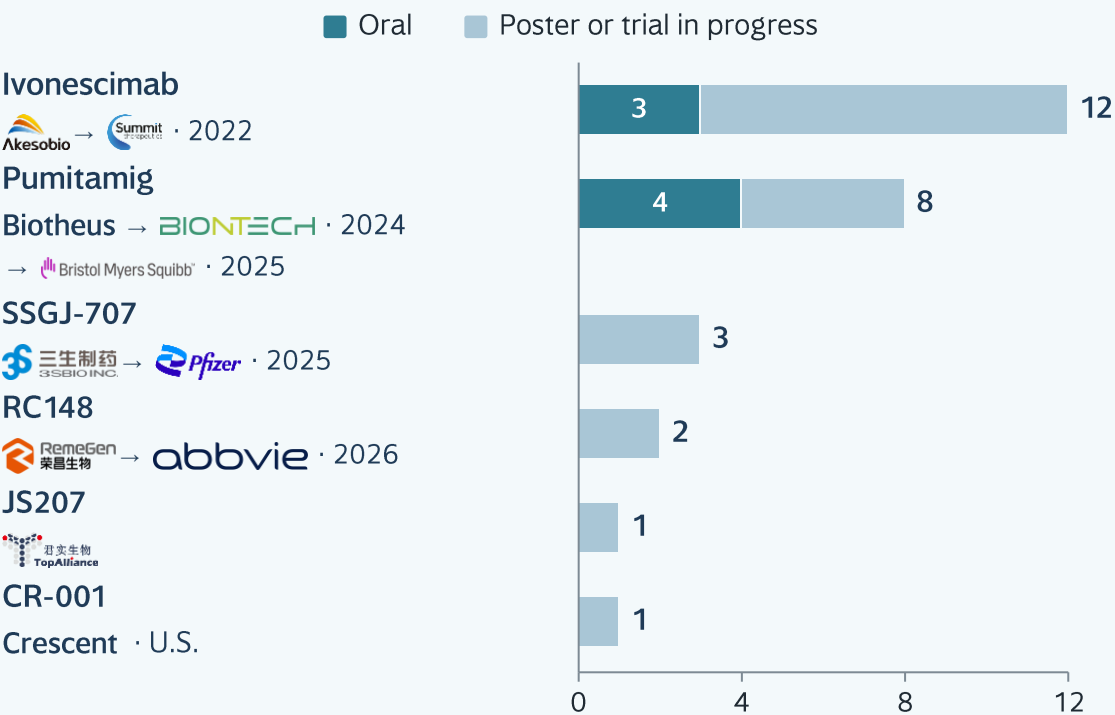
U.S. exclusivity ends 2028

Sleuth Insight: Since approval, Keytruda and Opdivo have run trials across tumors and lines. Their early-stage trials look like remaining lifecycle bets on new settings and combinations as U.S. exclusivity ends in 2028.

PD-(L)1 × VEGF bispecifics now go head-to-head against PD-(L)1 drugs

20% of their abstracts are presented orally vs 6% overall, and 22 of 27 presentations sit outside NSCLC

PD-(L)1 × VEGF presentations at ESMO 2026, by agent (27)



The 5 trials randomized against a PD-(L)1

Trial	Bispecific vs PD-(L)1 control	Tumor · line · phase	Status
HARMONi-GI1 (LBA8) 	Ivonescimab + chemo vs durvalumab + chemo	Biliary tract · 1L · Ph3	OS met at topline
2660P 	SSGJ-707 + chemo vs tislelizumab + chemo	Lung · 1L · Ph2	Response 75% vs 45%, non-squamous
2910P 	RC148 + RC118 vs toripalimab + RC118	Gastric · later line · Ph2	Response 57% vs 38%, 21 per arm
Symbiotic-GYN-18 	PF-08634404 + chemo vs pembrolizumab + chemo	Endometrial · 1L · Ph3	In progress
ROSETTA Gastric-204 	Pumitamig + chemo vs nivolumab + chemo	Gastric · 1L · Ph2/3	In progress

- Ivonescimab beat pembrolizumab, each administered as a monotherapy, in PD-L1+ lung cancer in China (PFS HR 0.51, interim OS HR 0.73)
- The FDA decision on ivonescimab in EGFR-mutant lung cancer is due on November 14th, 2026

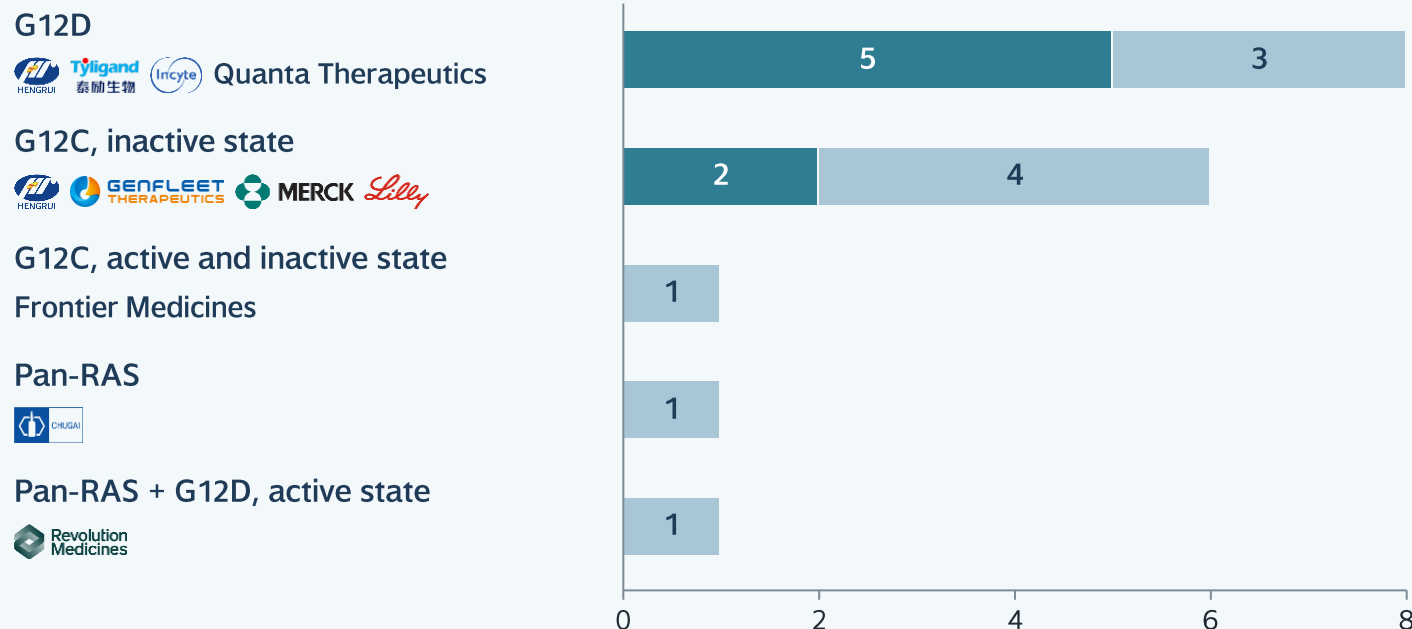
Sleuth Insight: Five ESMO 2026 trials test these bispecifics against a PD-(L)1, two against pembrolizumab or nivolumab. This suggests a class built to replace PD-1 drugs, who critically face the loss of patent exclusivity in the U.S. in 2028.

G12D drugs lead ESMO 2026 KRAS-inhibitor abstracts, mostly in combinations

35% of their clinical abstracts are presented orally vs 6% overall, and G12D leads with 8 of 17

The 17 clinical KRAS-inhibitor abstracts, by mechanism

■ China-originated ■ Japan- and West-originated



Combinations

13 of 17 pair the KRAS inhibitor with another drug, most often chemotherapy (8), a PD-(L)1 (6) or an EGFR antibody (5)

Front line

8 of 17 include first-line or perioperative patients, including each of the 4 lung cancer abstracts

Sotorasib showed no OS gain over docetaxel in lung cancer (HR 1.01), and daraxonrasib, a pan-RAS inhibitor, won FDA approval in pancreatic cancer in Aug 2026 (OS HR 0.40)

Sleuth Insight: KRAS development is racing toward combinations, but pivotal programs at ESMO 2026 have mostly yet to follow, with 3 of the 4 phase 3s in progress testing a single drug.

ADCs rise from 6% of abstracts to 24% of late-breakers at ESMO 2026

15 of the 22 ADC late-breakers test China-originated ADCs, 3 of the 4 Presidential ones

Abstracts

ADCs appear in **6%** (239 of 4,275) of abstracts



Late-breakers

ADCs are **24%** (22 of 91) late-breakers, and **68%** (15 of those 22) are China-originated



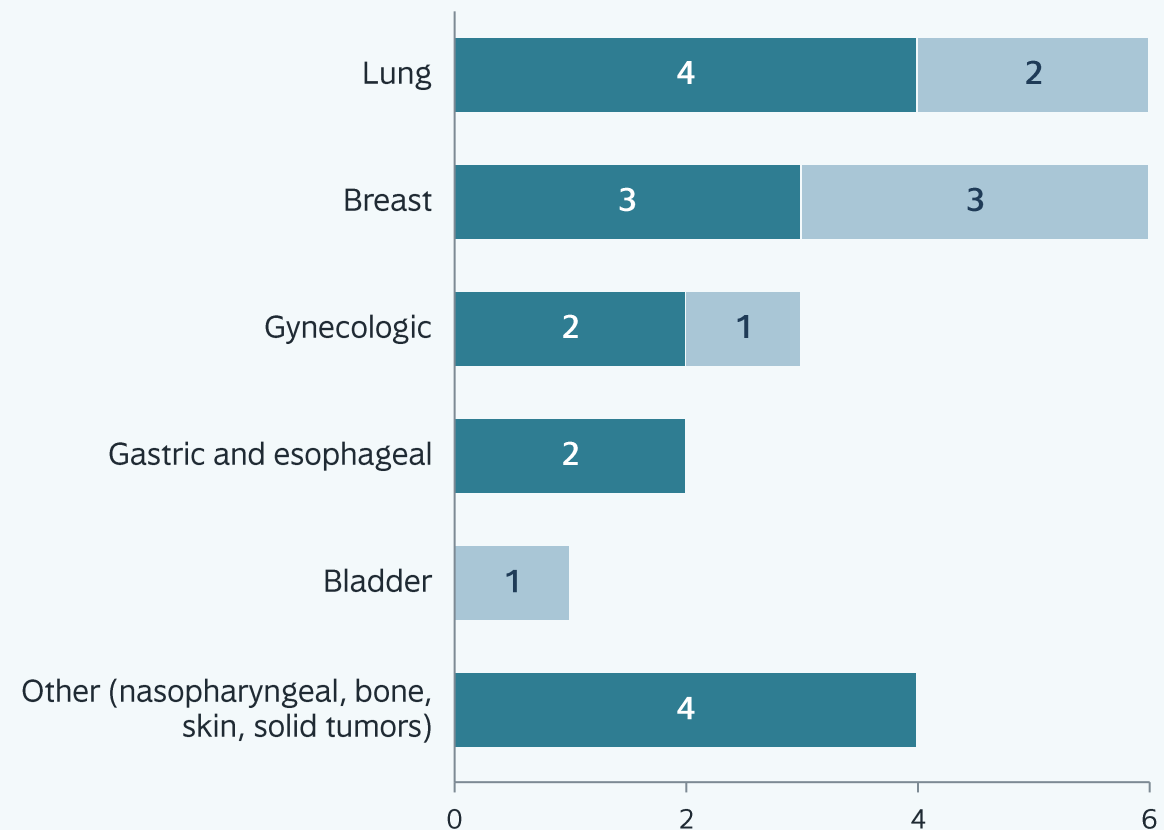
Presidential late-breakers

ADCs are **33%** (4 of 12) Presidential late-breakers, and **75%** (3 of those 4) are China-originated

The 22 ADC late-breakers by tumor

■ China-originated

■ Japan- and West-originated



China-originated ADCs supply 12 of the 14 phase 3 ADC readouts at ESMO 2026

Toplines separate winners from losers, as 12 of 14 met a primary endpoint, 1 was mixed and 1 did not

Primary endpoint at topline = result the company announced before ESMO. No hazard ratios released

All 22 ADC late-breakers, by agent

■ U.S. or European licensee

□ Marketed in the U.S.

Agent	Target	Originator → licensee · year	Late-breaker: tumor · line · phase	Primary endpoint at topline	Other ESMO 2026 abstracts
China-originated ADCs · 12 agents, 15 late-breakers					
Sacituzumab tirumotecan	TROP2	 KELUN-BIOTECH 科伦博泰 →  MERCK · 2022	EGFR-mutant NSCLC · 2L+ · Ph3 PD-L1-negative NSCLC · 1L · Ph3 Endometrial · 2L+ · Ph3	PFS met PFS met OS + PFS met, subgroup	2 orals · 6 posters
Izalontamab brengitecan	EGFR×HER3	 Biokin Pharma →  Bristol Myers Squibb · 2023	HR+/HER2- breast · 2L+ · Ph3 EGFR-mutant NSCLC · 2L+ · Ph3	PFS met PFS met	1 oral · 1 poster
Sonesitaturg vedotin	CLDN18.2	KYM Biosciences →  AstraZeneca · 2023	Gastroesophageal · 2L+ · Ph3	OS met, PFS not met	1 poster
Risvutaturg rezetecan	B7-H3	 HANSHI →  GSK · 2023	Osteosarcoma · 2L+ · Ph3	PFS met	4 posters
Mocertaturg rezetecan	B7-H4	 HANSHI →  GSK · 2023	Ovarian · 2L+ · Ph1	–	1 oral · 2 posters
Disitamab vedotin	HER2	 RemeGen 莱恩生物 →  Pfizer · 2021	Extramammary Paget's · Ph2	–	2 orals · 16 posters
MRG007	CDH17	 乐普生物 →  ARRIVENT · 2025	Solid tumors · 2L+ · Ph1	–	–
Tambotaturg pelitecan	B7-H3	 MediLink Therapeutics →  Roche · 2026	Nasopharyngeal · 2L+ · Ph3	ORR met, 1 of 2	2 posters
Arcotaturg tavatecan	CLDN18.2	Innovent →  Takeda · 2025	Gastric · 2L+ · Ph3	Primary met	–
Trastuzumab rezetecan	HER2	 HENGSHI →  glenmark · 2025	HER2-low breast · Ph3	PFS met	2 posters
Rolditamig deuderuxtecan	HER2	CTTQ →  Cipla · 2026	HER2-low breast · Ph3	PFS met	1 oral
Ruzaltaturg rezetecan	HER3	 HENGSHI · no announced licensee	EGFR-mutant NSCLC · 2L+ · Ph3	PFS met	2 posters
Japan- and West-originated ADCs · 5 agents, 7 late-breakers					
Trastuzumab deruxtecan Marketed	HER2	 Daiichi-Sankyo +  AstraZeneca	HR+ early breast · neoadjuvant · Ph2 HER2-mutant NSCLC · 1L · Ph3 secondary HER2+ breast · 1L · Ph3 secondary	– – –	3 orals · 29 posters
Datopotamab deruxtecan Marketed	TROP2	 Daiichi-Sankyo +  AstraZeneca	Triple-negative breast · 1L · Ph3 secondary	–	4 posters
Enfortumab vedotin Marketed	Nectin-4	 astellas +  Pfizer	MIBC · perioperative · Ph3 (with durvalumab)	EFS + OS met	7 orals · 31 posters
Sigvotaturg vedotin	Integrin β6	 Pfizer	NSCLC · 2L+ · Ph3	OS not met	–
ZW191	FRα	 zymeworks	Ovarian · 2L+ · Ph1	–	–



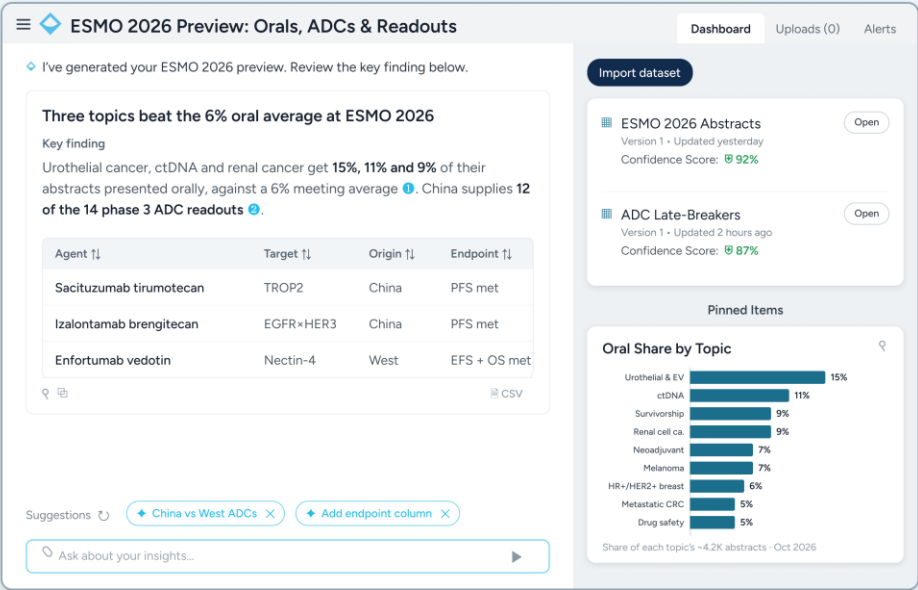
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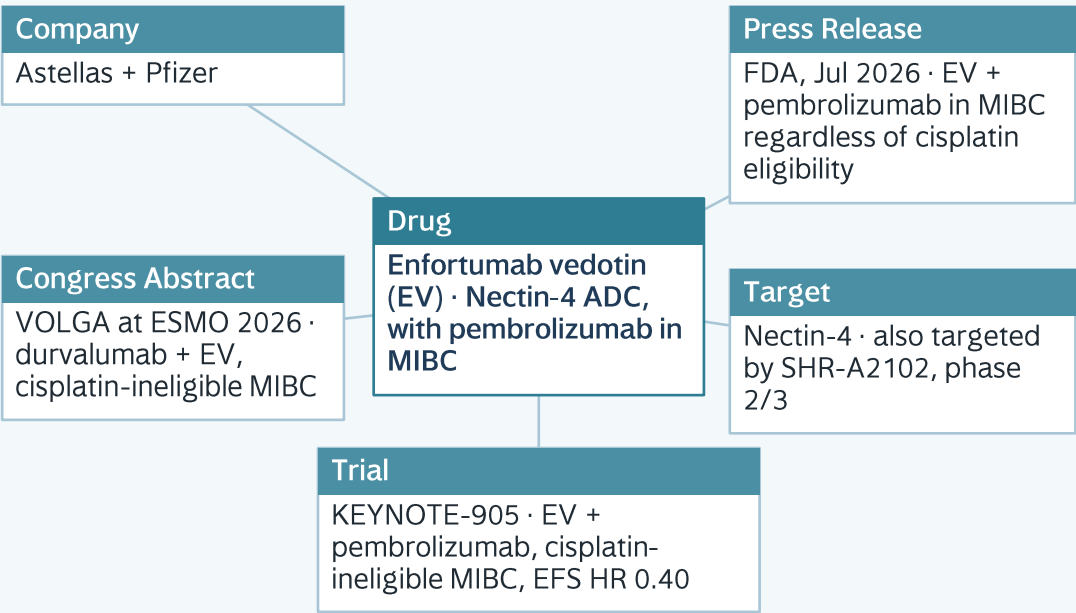
Main Takeaway: Urothelial, ctDNA and renal cancer win above-average oral shares at ESMO 2026, and ADCs are 24% of late-breakers, most China-originated.



Intelligence you can stand behind

Bring Sleuth your questions, and pre-connected intelligence surfaces automatically. Our knowledge graph connects data across the landscape, with full traceability.

Illustrative knowledge graph for enfortumab vedotin (EV)



Every claim traceable to source document

