23 Sep'25

DAY 2

WE ARE UNSTOPPABLE
Reigniting Erbitux in MEAR

Go Beyond 2025

5 mins	Opening and objectives	*Mohamed and Harshveer*
10 mins	**What makes our teams unstoppable in Oncology?**	*GMs (Ahmed, Moncef & Haitham) and Alena*
SCCHN		
5 mins	Introduction…	*Harshveer and Pauline*
10 mins	· **My story!**	*Head and Neck Cancer fighter (video)*
5 mins	Q/A	*All*
15 mins	· **Strategies in management of head and neck cancer**	*Professor Thorsten Füreder*
10 mins	Q/A	*All*
10 mins	**Strategy and Performance: Erbitux in SCCHN**	*Andrey, Pauline, Mohamed and Niklas*
5 mins	**Panel discussion:**	*Moderator: Mohamed and Harshveer*
15 mins	· **Behavioral segmentation and Messaging**	*Panel: Barbara, Andrey, Pauline, TRK, NA and NE*
10 mins	· **How to raise the bar in execution in SCCHN?** Q/A	*All*
10 mins	**Coffee break**	
CRC		
10 mins	**Strategy and Performance: Erbitux in CRC**	*Mohamed, Filippo and Niklas*
15 mins	**Panel discussion:** How to raise the bar in differentiation in CRC 1L LS RAS wt ?	*Moderator: Mohamed and Harshveer* *Panel: Barbara, Filippo, RUS, KSA, NA*
10 mins	Q/A	*All*
5 mins	**Breakout room #1(RUS,IR,TRK)** **Differentiation vs NCB** **Introduction …** **Panel discussion** Q/A	*Moderator: Patricia* *Panel: Barbara, Harshveer, Ihab & Patricia.* *Country BUH, Med., Reg. and MAP*
15 mins	**Breakout room #2 (rest of MEAR)** **Reviving Rechallenge** **Introduction …** **Panel discussion** Q/A	*Moderator: Mohamed and Filippo* *Country: MKTG and Medical*
10 mins	**Insights from the 2 groups:** Group lead Closing day 2	

What makes us unstoppable in Oncology?

Alena Lobodina

Global Commercial Operations Director

Ahmed Abo-Elfadl

Gulf GM

Haitham Habashi

Russia/CIS GM

Moncef Meklati

NA & FSA GM

Professor Thorsten Füreder

Medical University of Vienna, Austria

Patient Journey in R/M SCCHN

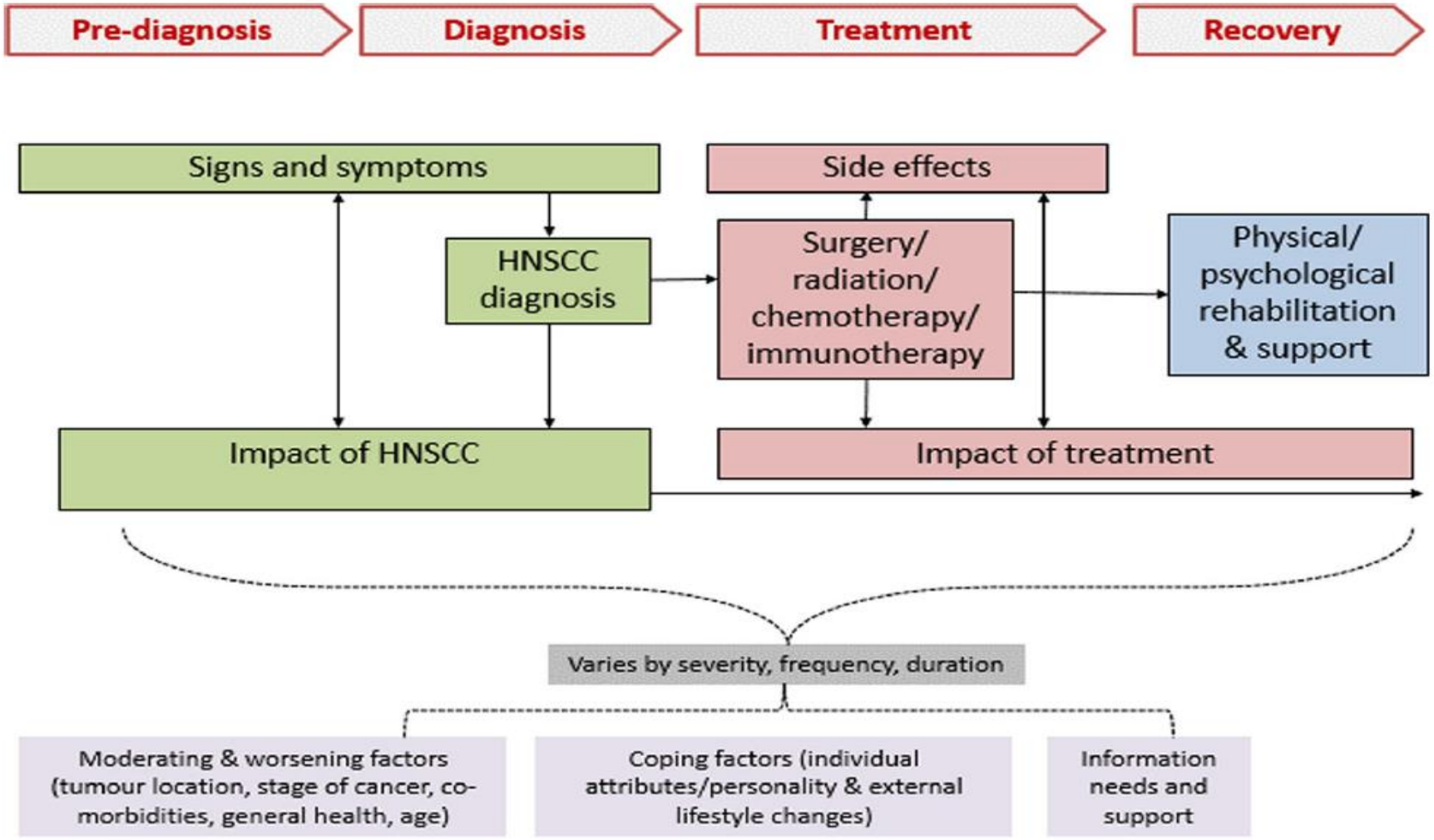
Assoc.Prof.PD.Dr.Thorsten Füreder

Department of Medicine I, Medical University of Vienna

Disclosure

Honoraria or Advisor: MSD,Merck, BMS, BI, Roche, Sanofi, Amgen, Takeda, Invios; Janssen, Ely Lilly, Pierre Fabre, Pharma Mar; Pfizer, Daiichi, Beigene; Astra Zeneca

Patient Journey in HNSCC



Degboe et al.; Journal of Patient Reported Outcomes 20218

Patient Case

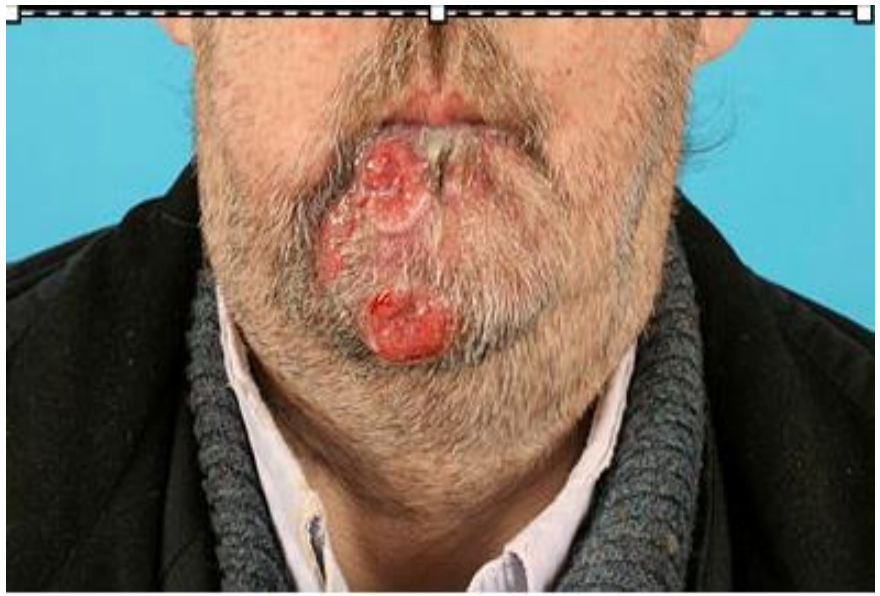
53 year old male patient

ECOG: 0

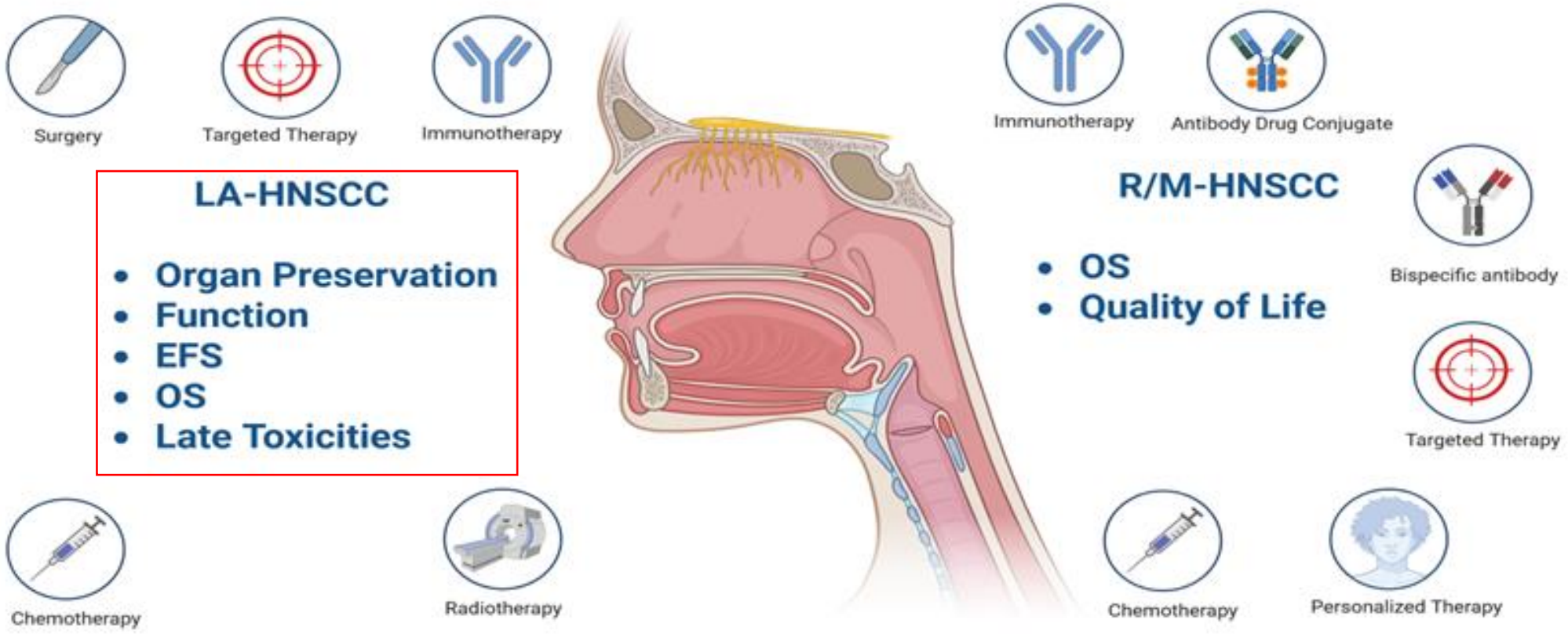
Oral cavity carcinoma cT4,cN2c,M0

Histology: Squamous Cell Carcinoma; CPS: 10

Medical History:
Smoker 20py
Chronic Pancreatitis



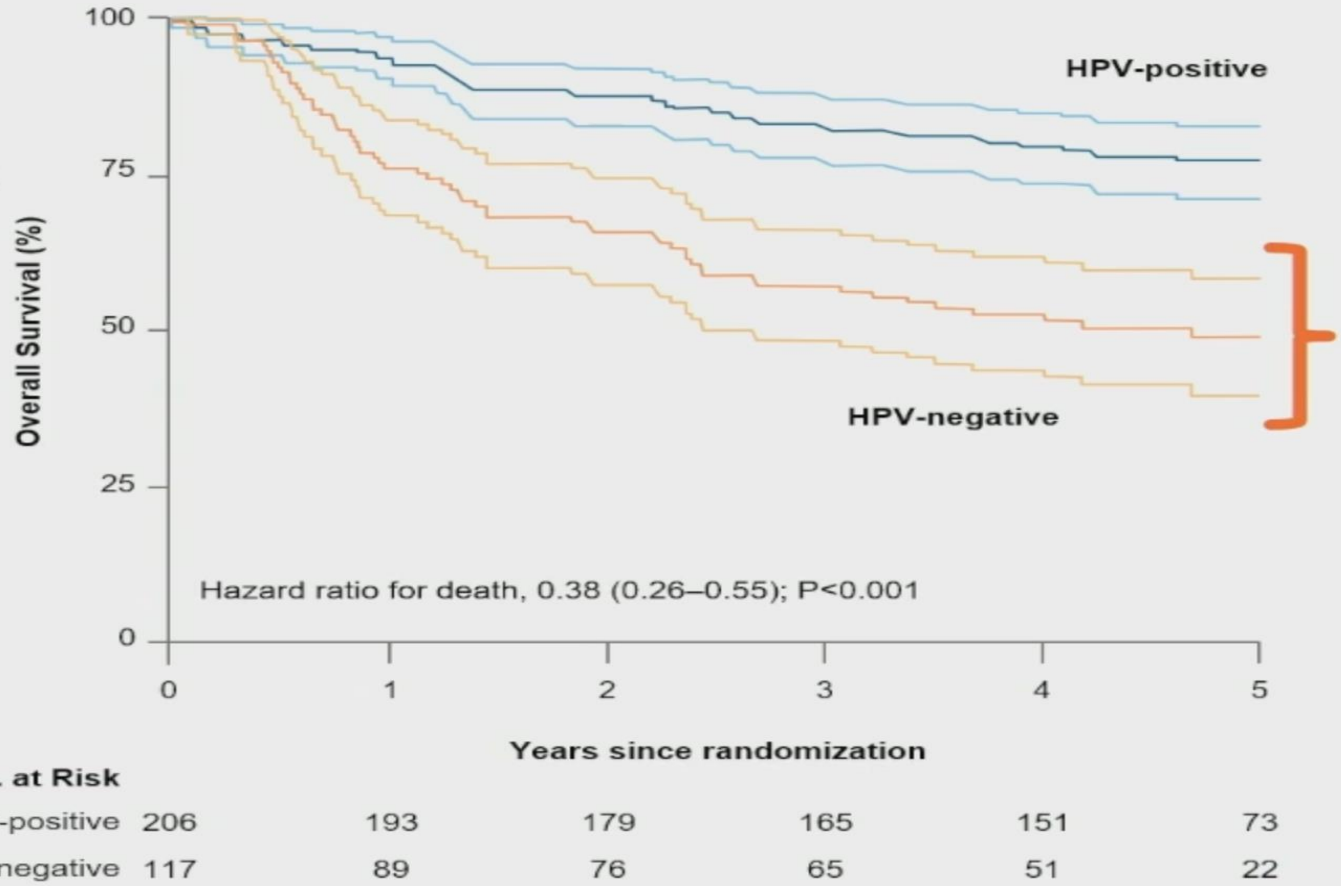
Treatment Considerations in HNSCC



Created with Biorender

Consideration: OS in LA-HNSCC

- **Survival for locoregionally advanced (LA) HPV negative (-) HNSCC remains poor with five-year survival of ~50%.**[1]
- Standard multimodality therapy is associated with substantial acute and late treatment-related toxicity.[2]
- Treatment optimization that improves survival while reducing treatment-related toxicity is urgently needed.



[1]Ang KK, et al. N Engl J Med 2010;363(1):24–35. [2]Machtay M, et al. Journal of Clinical Oncology 26:3582-3589, 2008

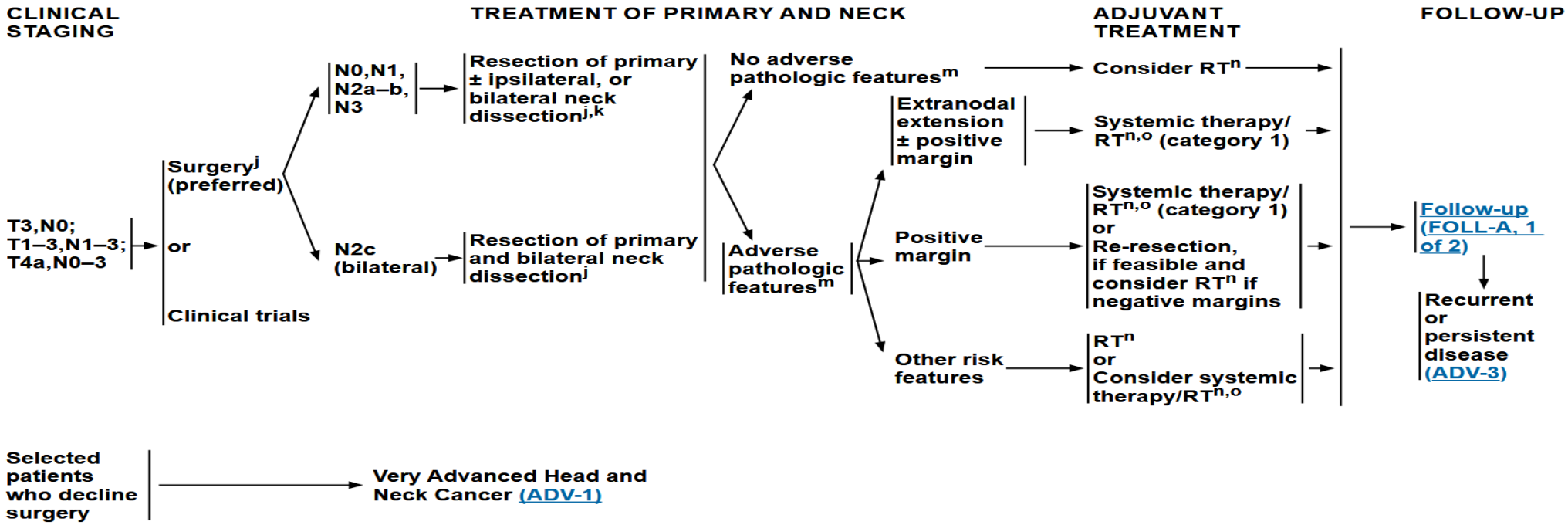
Current Guidelines LA-OSCC

National Comprehensive Cancer Network®

NCCN Guidelines Version 3.2025
Cancer of the Oral Cavity (Including Mucosal Lip)

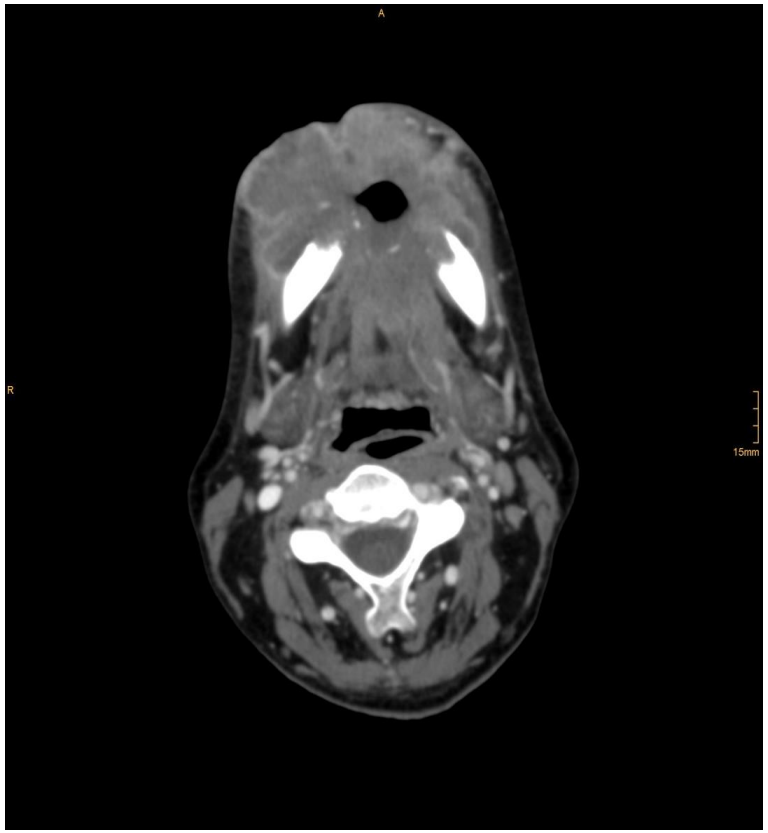
NCCN Guidelines Index
Table of Contents
Discussion

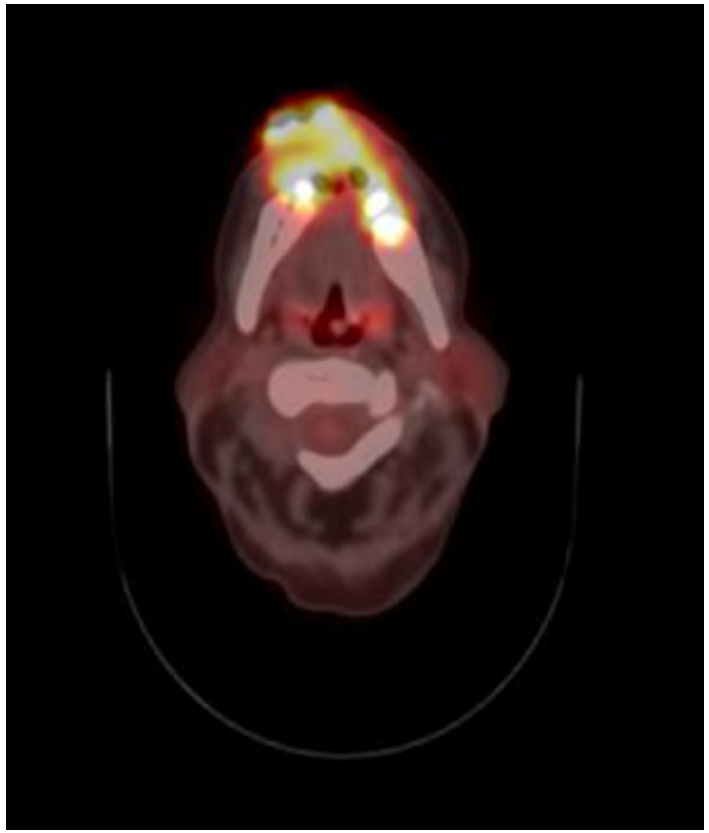
Buccal mucosa, floor of mouth, oral tongue, alveolar ridge, retromolar trigone, hard palate[a]

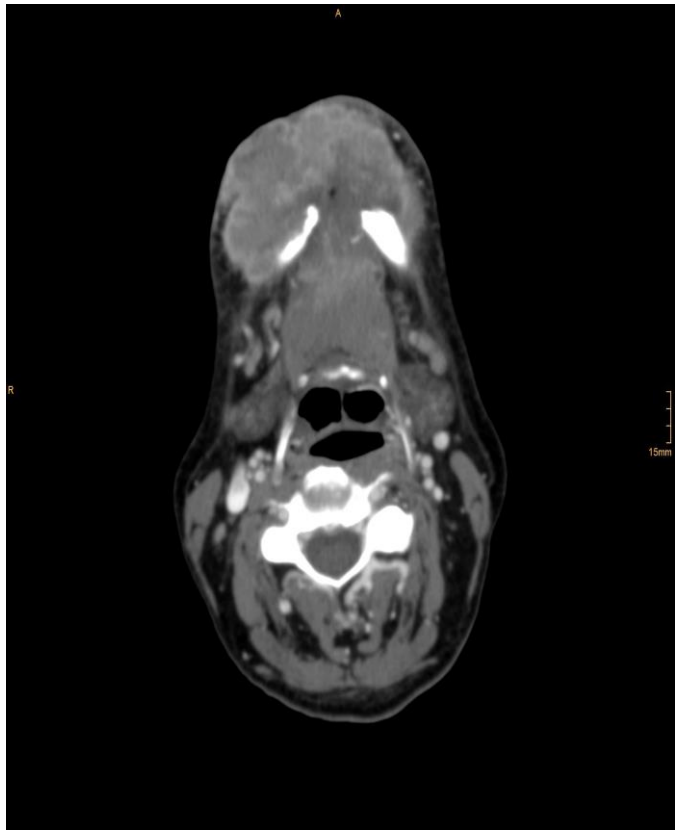


[a] Cutaneous squamous cell carcinoma of the vermilion lip is not included in this guideline. See NCCN Guidelines for Squamous Cell Skin Cancer.
[j] Principles of Surgery (SURG-A).
[k] Neck dissection is generally not indicated for T1–3,N0 mucosal lip.
[m] Adverse pathologic features: extranodal extension, positive margins, close margins, pT3 or pT4 primary, pN2 or pN3 nodal disease, nodal disease in levels IV or V, perineural invasion, vascular invasion, and lymphatic invasion (Discussion).
[n] Principles of Radiation Therapy (OR-A).
[o] Principles of Systemic Therapy for Non-Nasopharyngeal Cancers (SYST-A).

Imaging

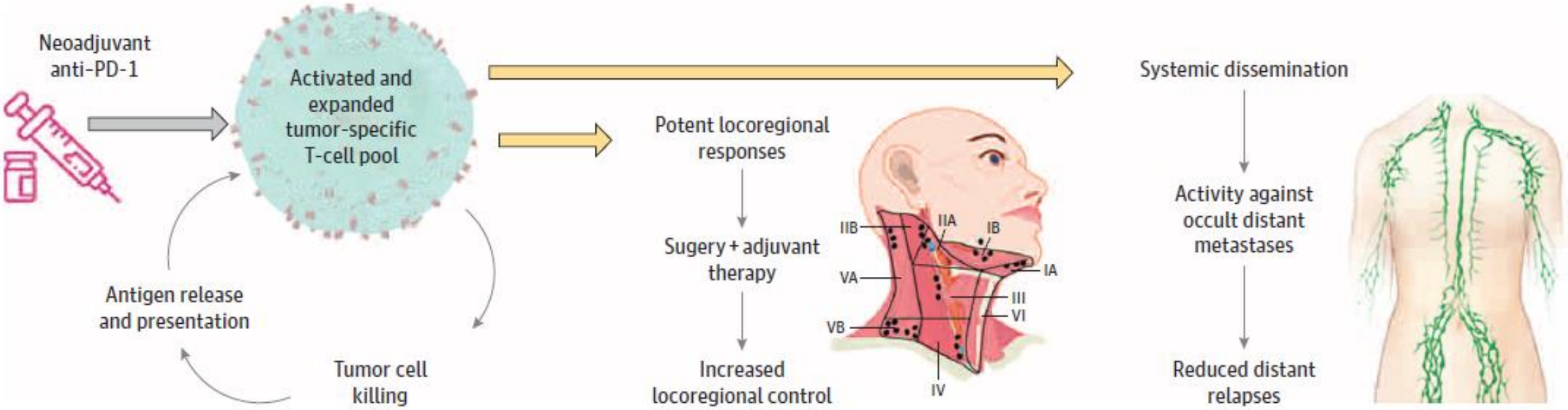






Images courtesy of Prof. Nemec

Consideration: Neoadjuvant Immunotherapy



Contrera et al; JAMA Otolaryngology Head and Neck Surgery 2025

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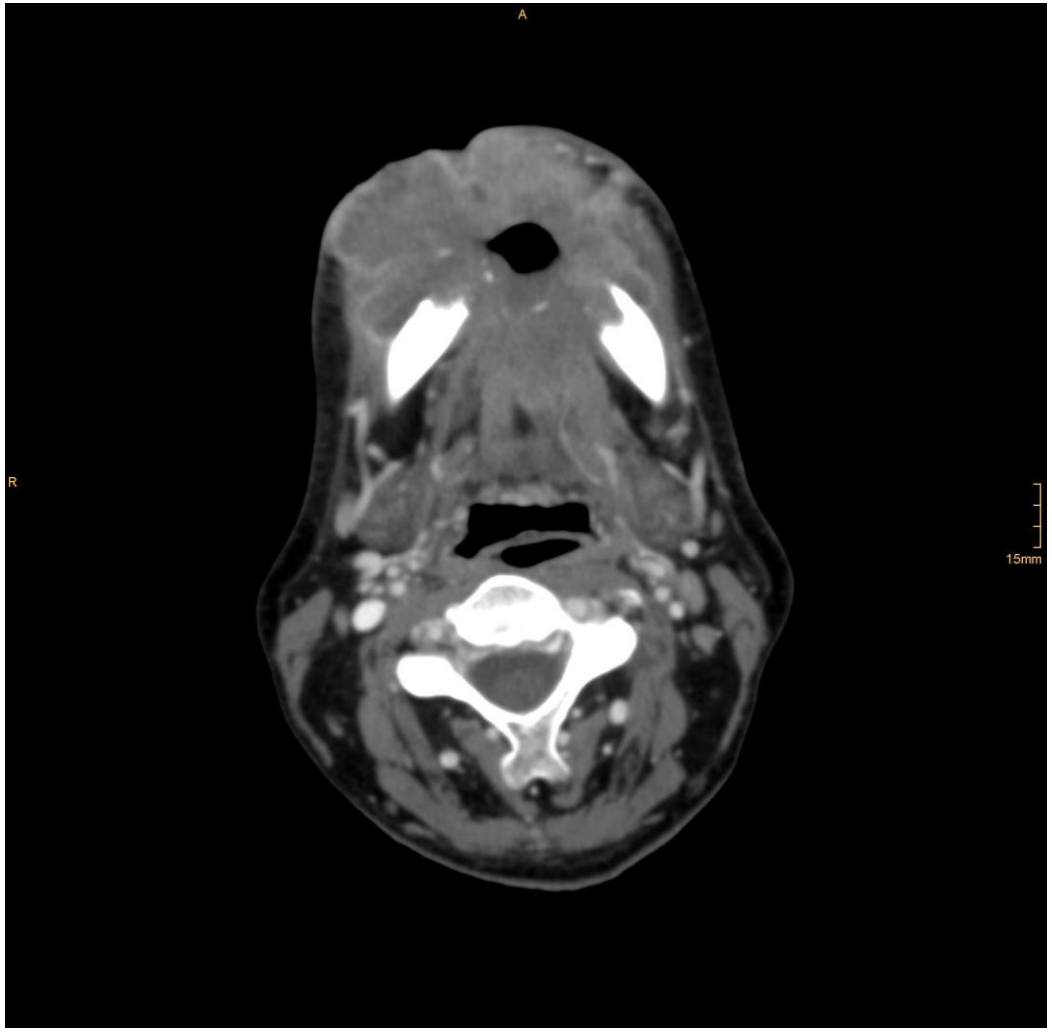
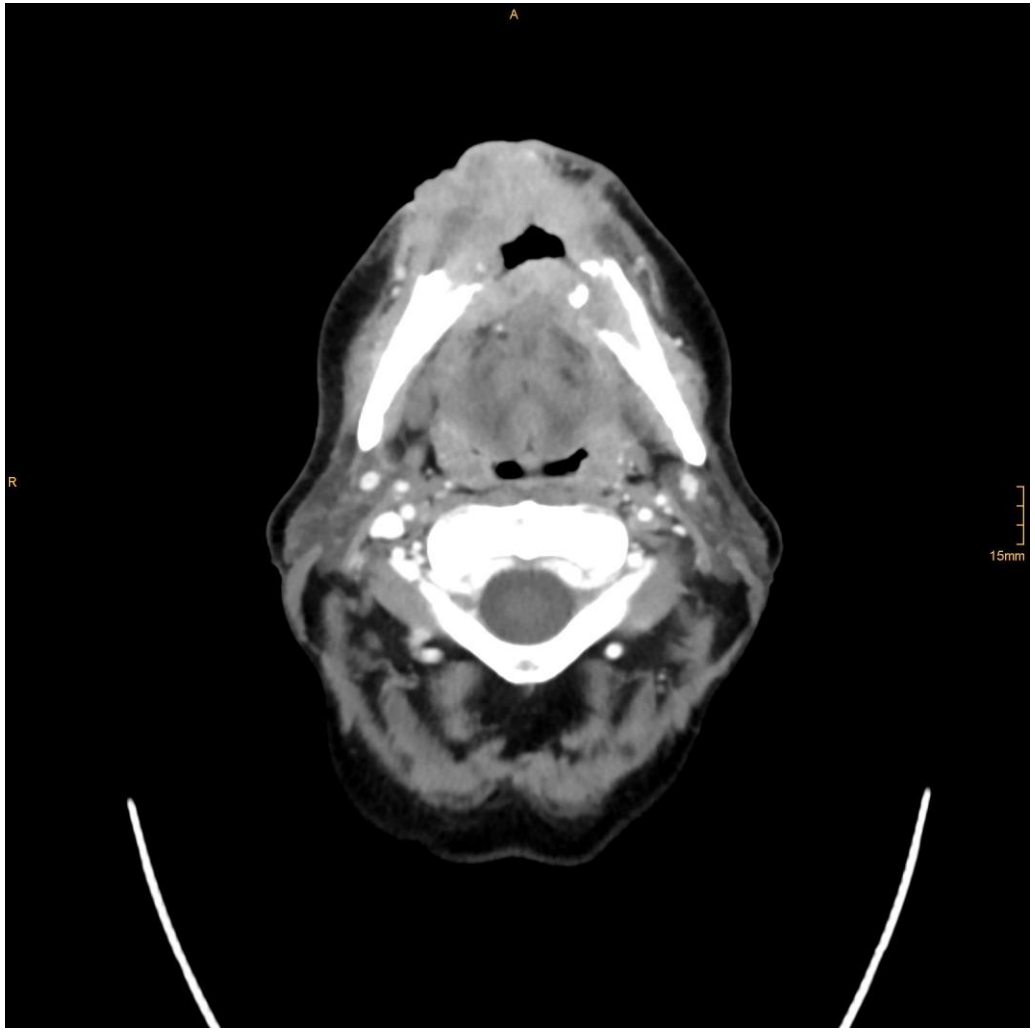
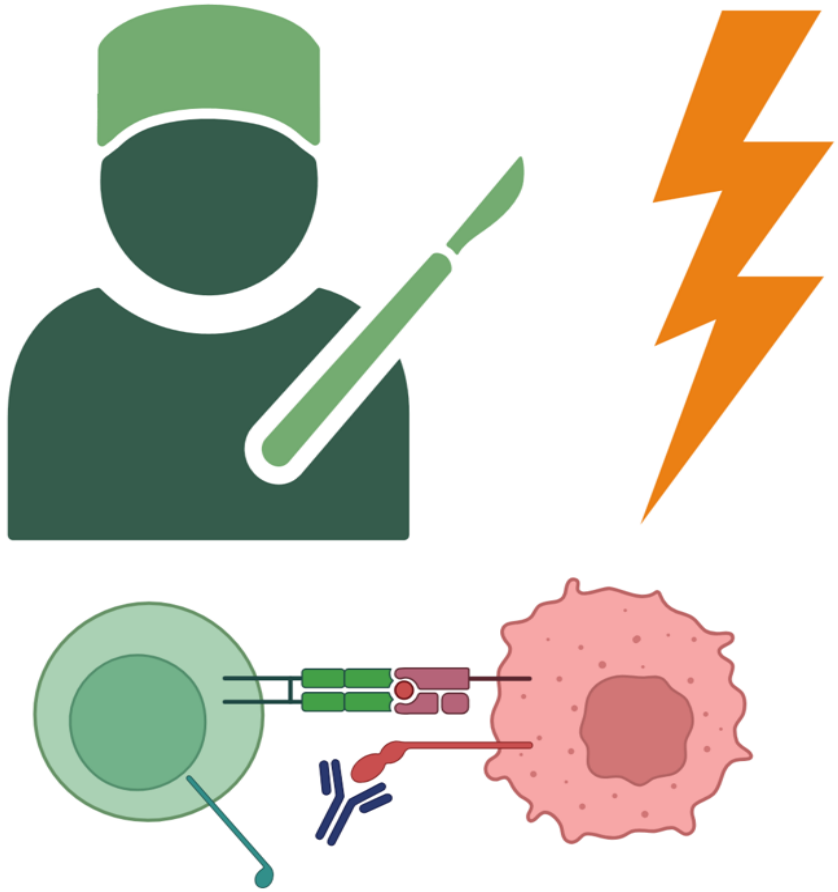


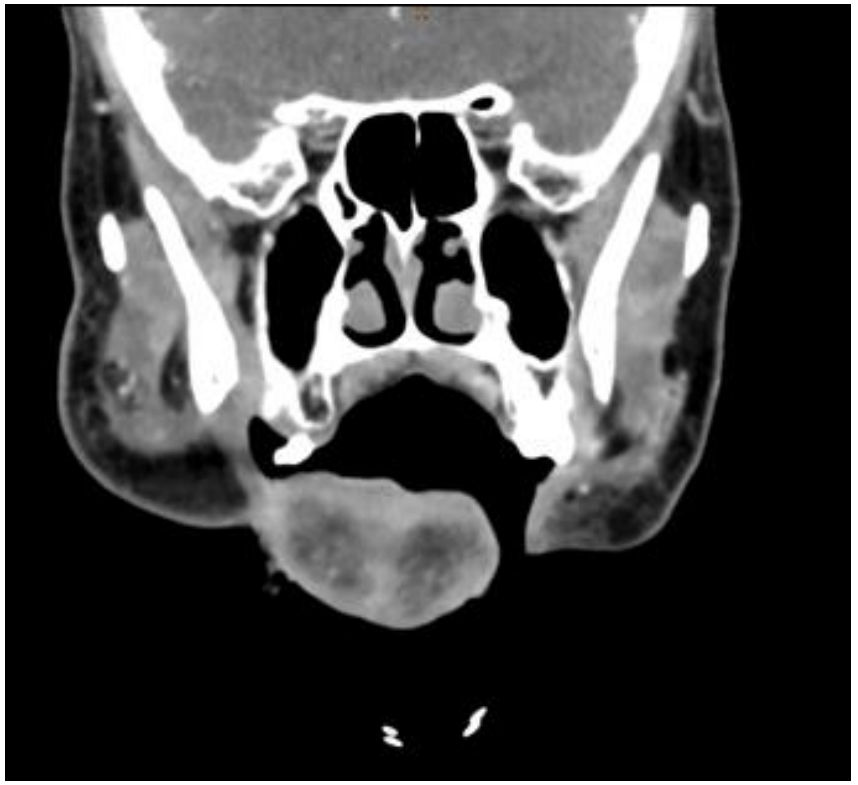
Baseline



After Immunotherapy

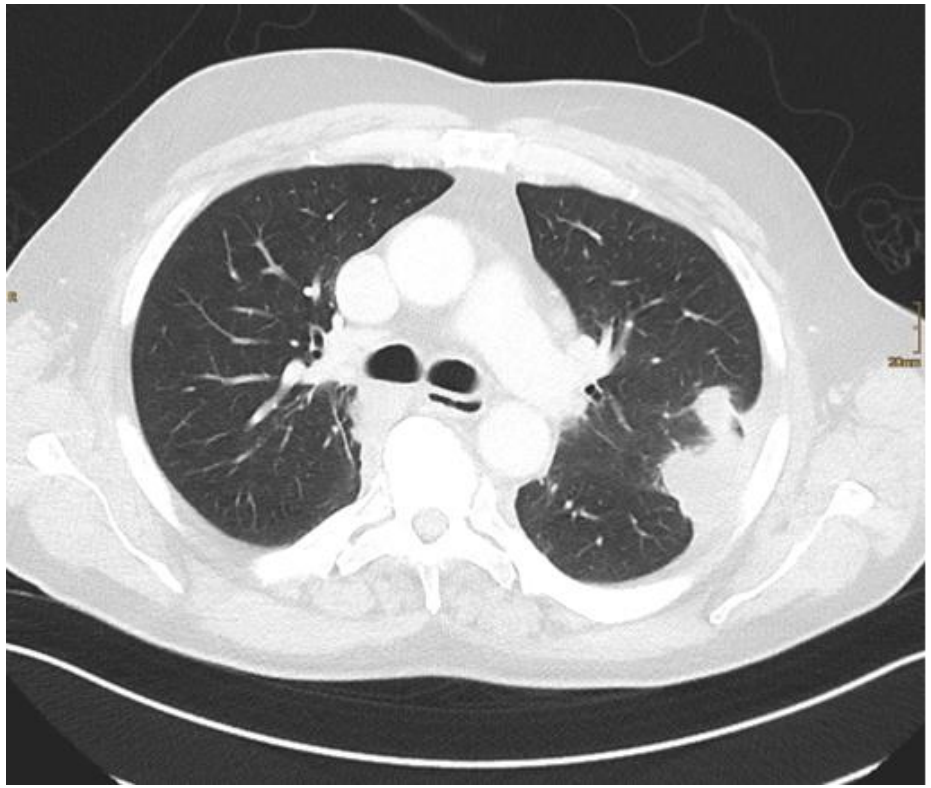
Imaging





Therapy completed

Recurrence



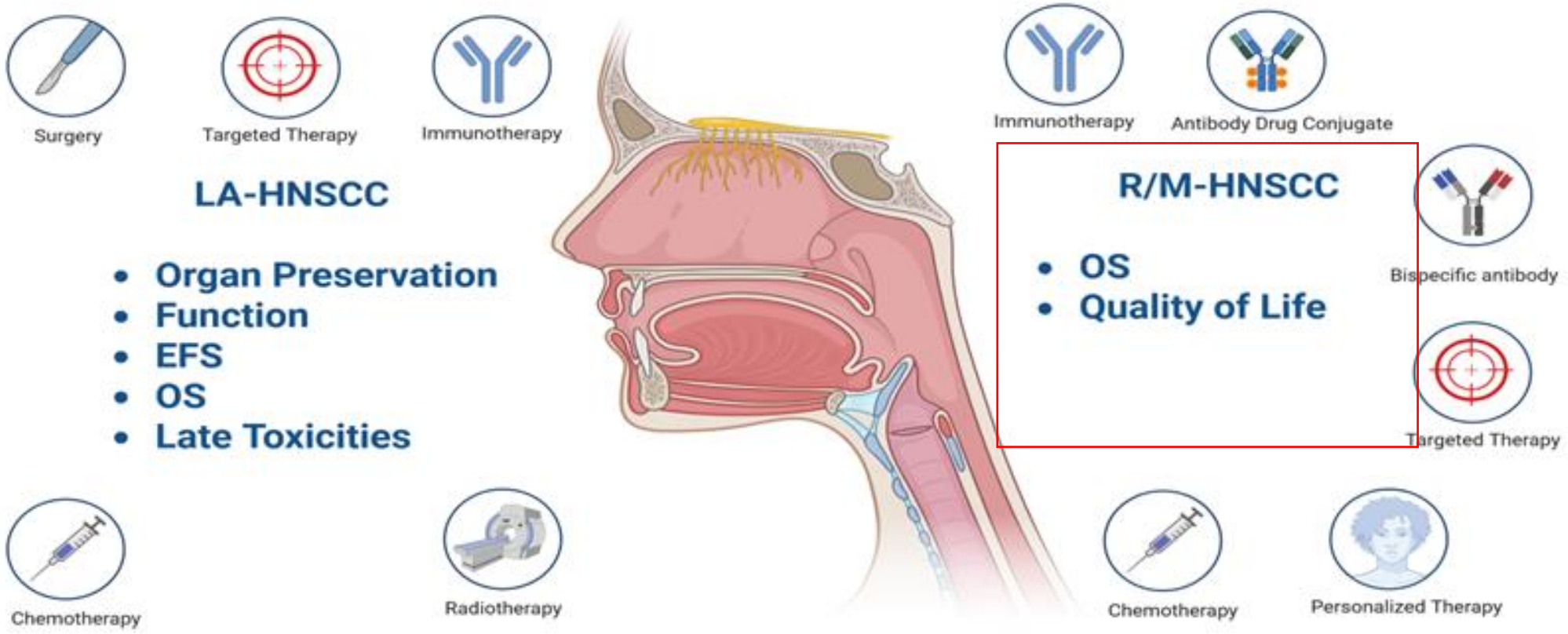
Distant recurrence after 1 year:

Histology: Squamous Cell Carcinoma; CPS: 20

ECOG: 0

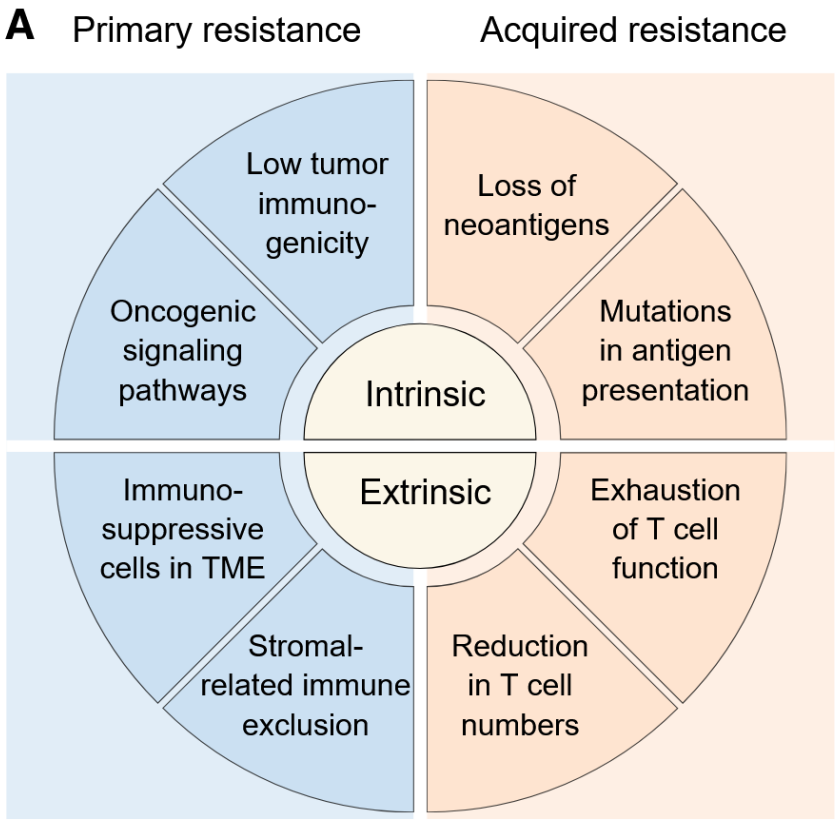
Images courtesy of Prof. Nemec

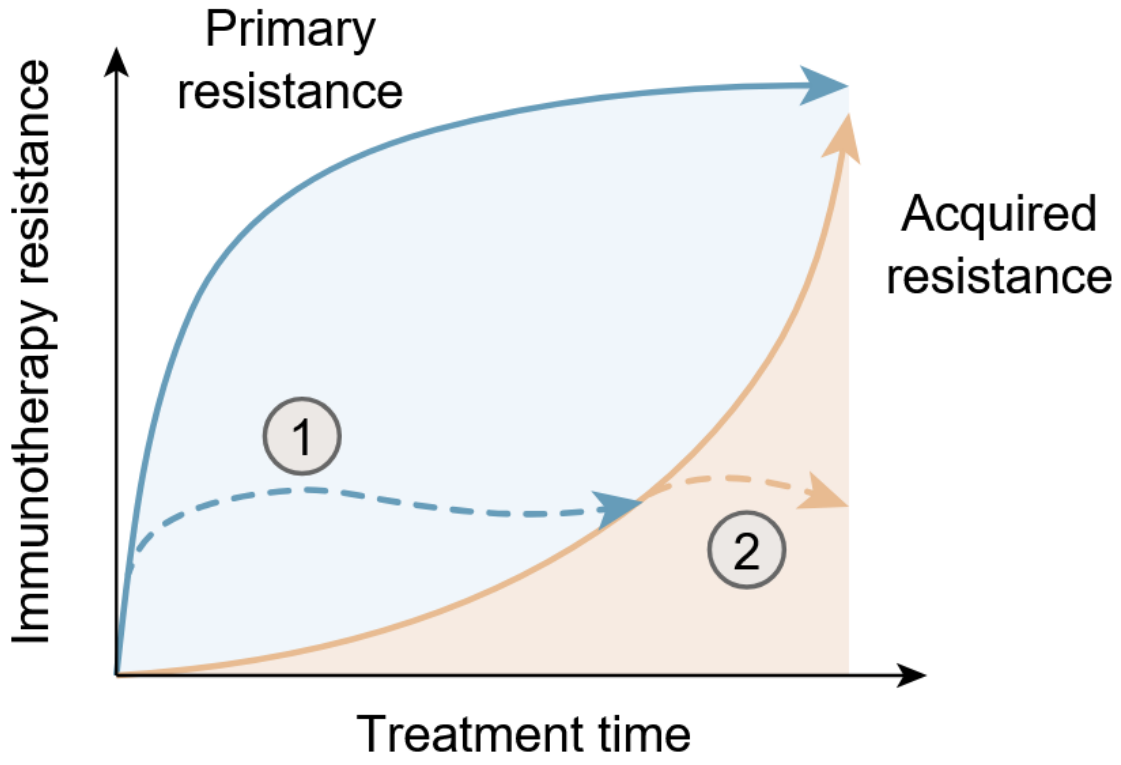
Treatment Considerations in HNSCC



Created with Biorender

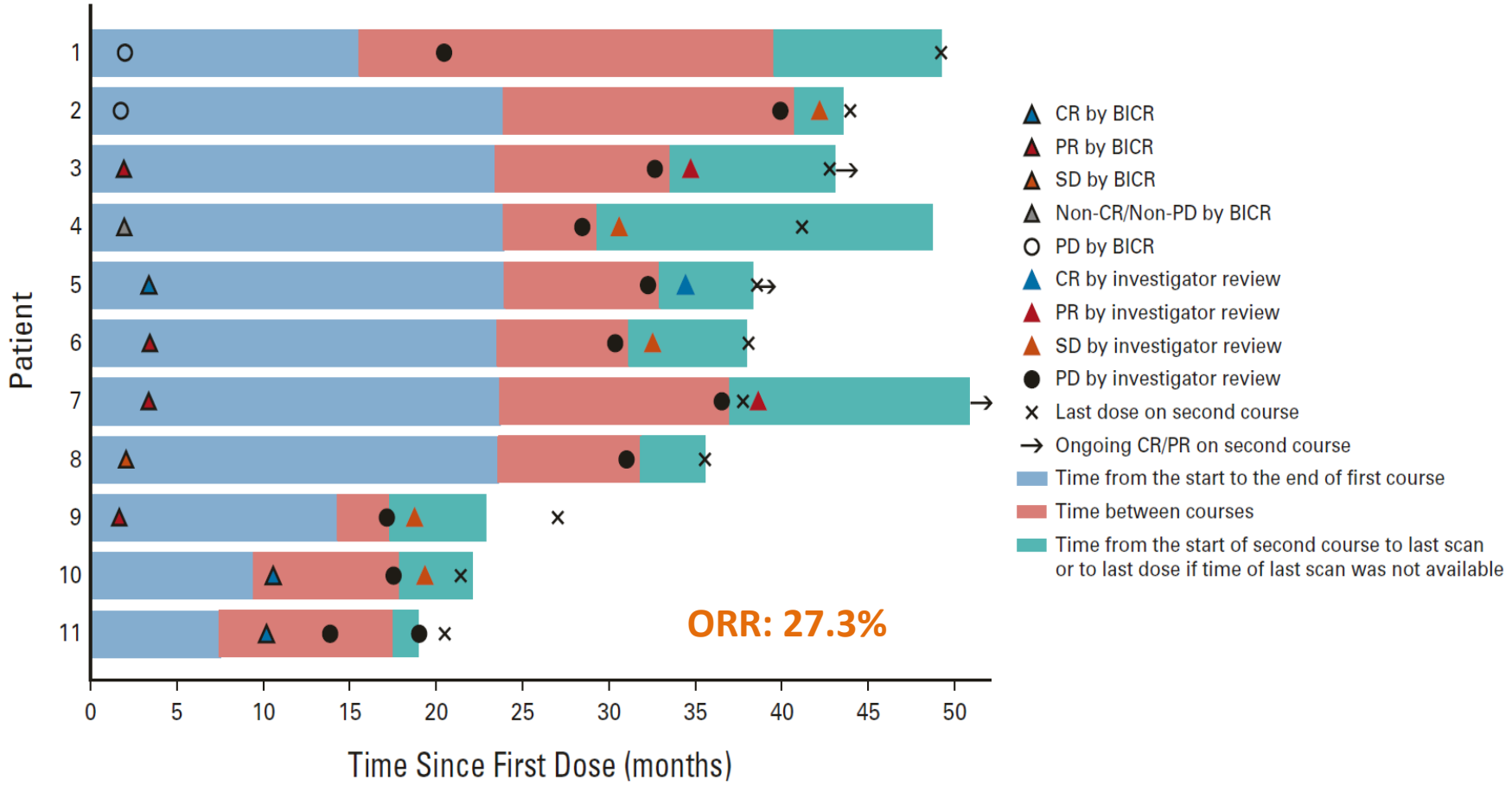
Consideration: Secondary Resistance





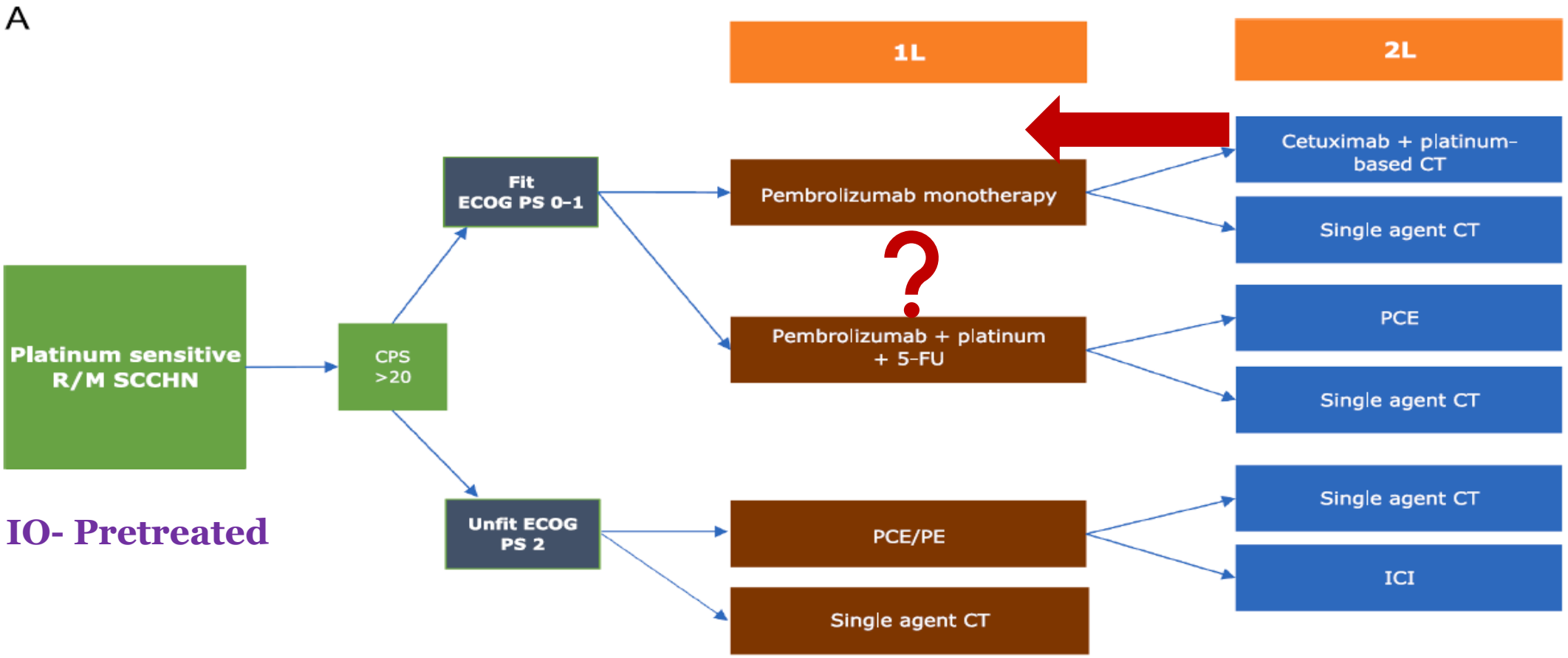
Kang et al.; Cell Reports Medicine 2025

Consideration: Keynote 48
Second Course Pembro- limited efficacy



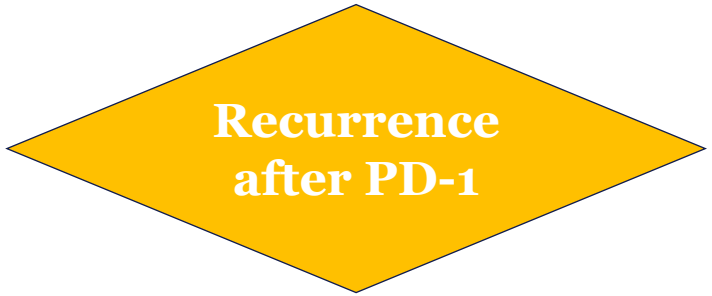
Harrington,.., Fuereder et al.; JCO 2022

Consideration:



Szturz,Fuereder et al.; Cancer Treatment Reviews 2025

Decision making R/M HNSCC



Platinum/Taxane+ Cetuximab

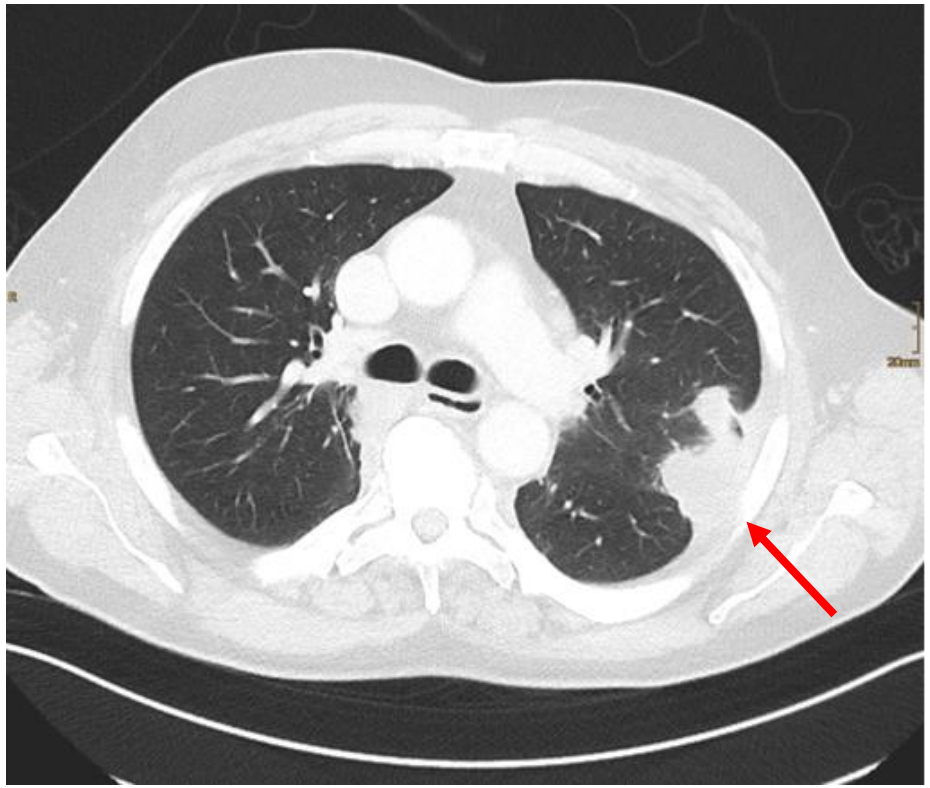
Pros: higher ORR; OS
Cons: Toxicity

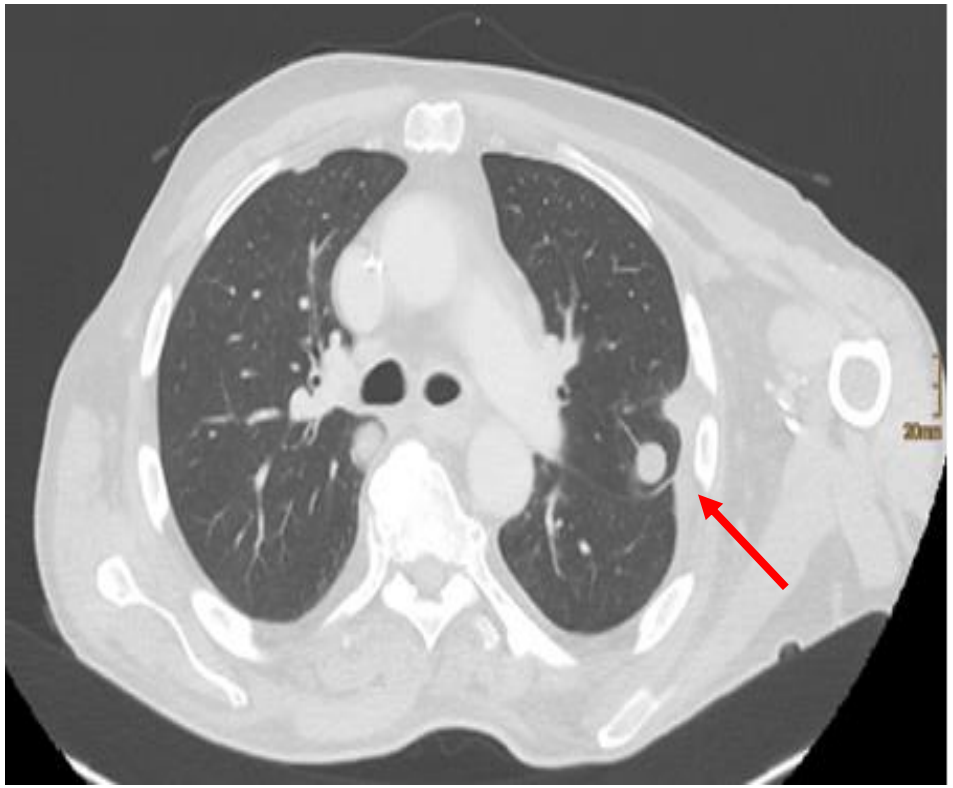
IO Re-challenge

Pros: tolerated as monotherapy
Cons: Benefit?

Clinical Trial

Imaging

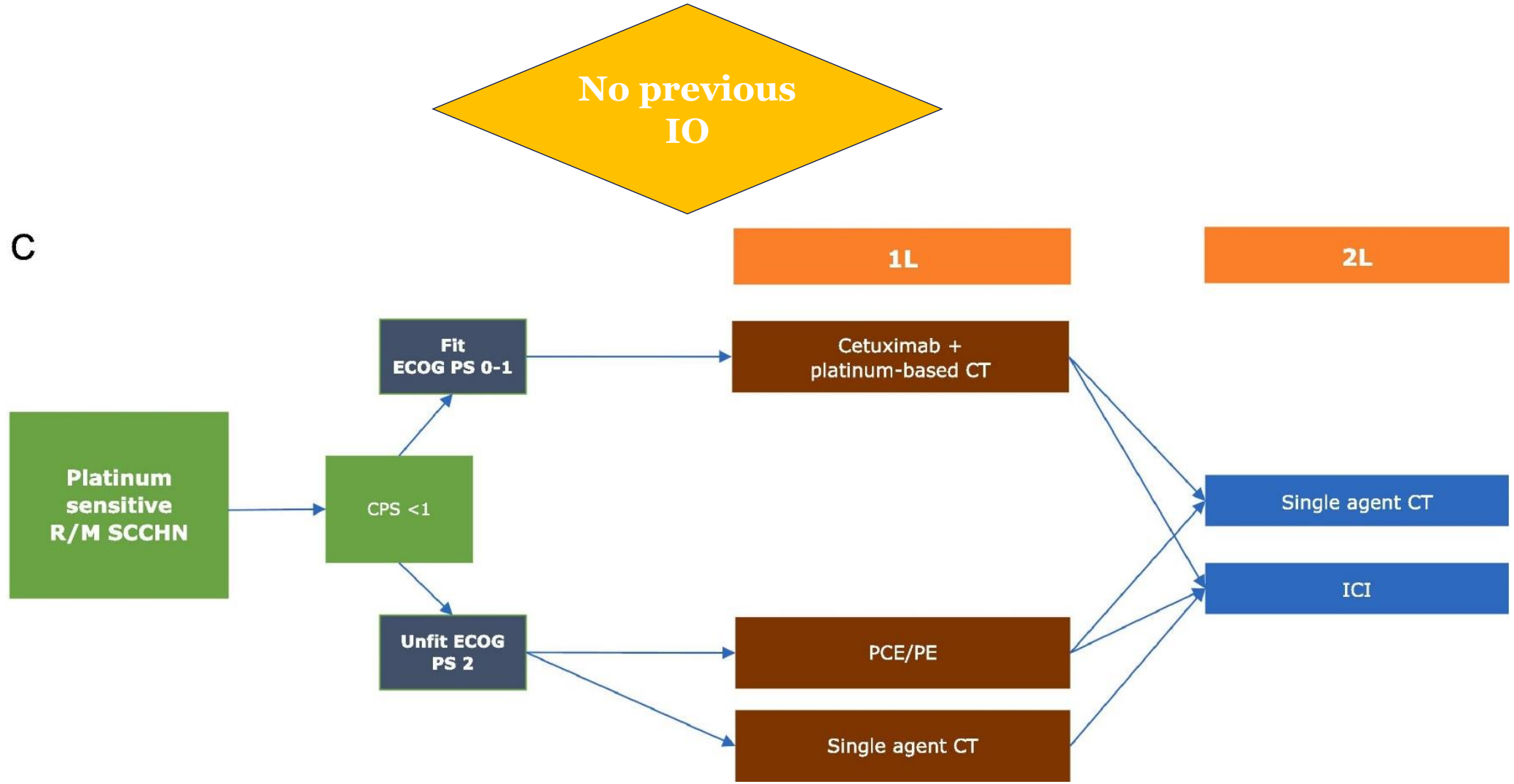




Baseline

After 4 cycles chemo-cetuximab

Decision making R/M HNSCC

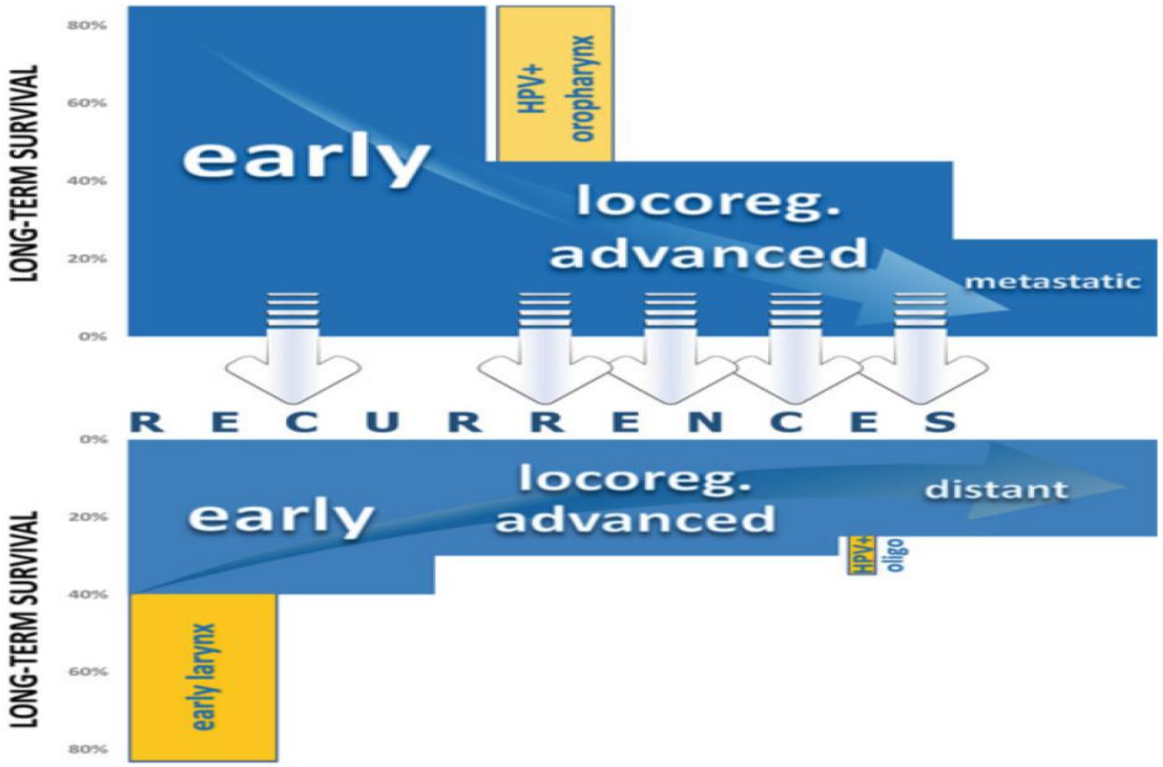


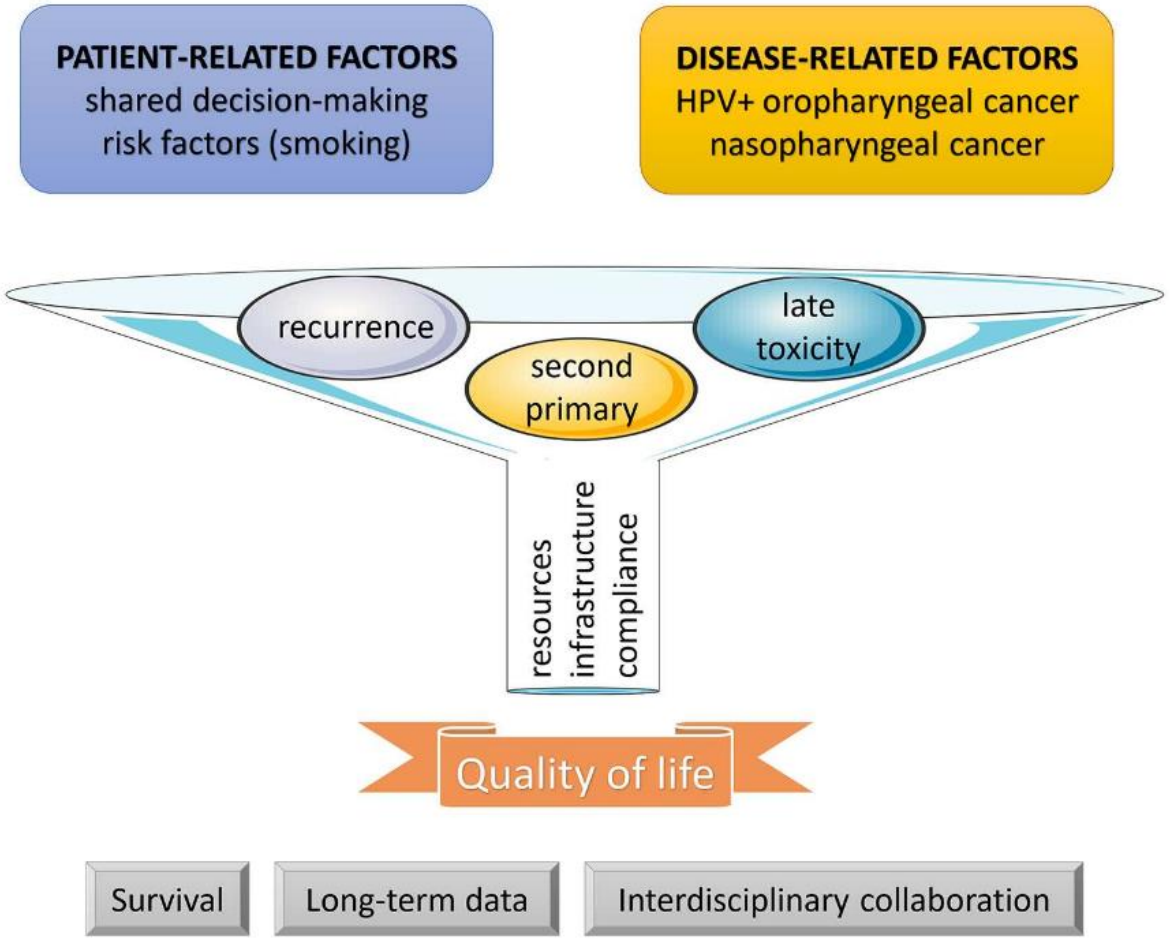
Szturz,Fuereder et al.; Cancer Treatment Reviews 2025

Decision making R/M HNSCC

Szturz,Fuereder et al.; Cancer Treatment Reviews 2025

Optimising OS in HNSCC patients





Szturz and Vermorken, Critical Issues in Head and Neck Oncology 2023 and Frontiers in Oncology 2020

Discussion


MEDIZINISCHER UNIVERSITÄTSCAMPUS
MEDIZINISCHE UNIVERSITÄT WIEN
Allgemeines Krankenhaus der Stadt Wien

23 Sep'25

DAY 2

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Reigniting Erbitux in MEAR

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5 mins		Opening and objectives	*Mohamed and Harshveer*
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10 mins	CRC	Q/A	*All*
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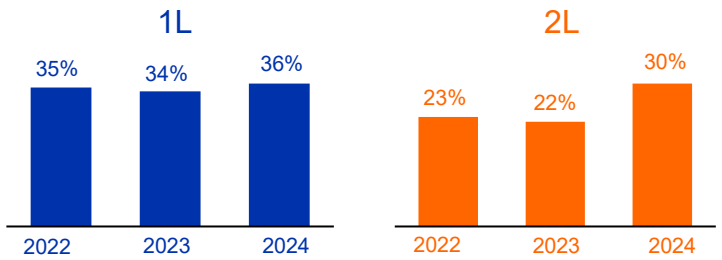
15 mins	CRC	**Breakout room #2 (rest of MEAR)** **Reviving Rechallenge** **Introduction …** **Panel discussion** Q/A	*Moderator: Mohamed and Filippo* *Country: MKTG and Medical*
10 mins		**Insights from the 2 groups:** Group lead Closing day 2	

2026 gives opportunities to reinforce Erbitux® positioning in the 1L R/M SCCHN

Stable market share dynamics

Recovering MS in 1L, growing MS in 2L



Growing RWE evidence

2020-2025: 6 completed trials, 19 RWE, 2 consensus publications (IT, FR)

2026: CETU-SEQ trial & Global Consensus planned

Potential landscape changes

KEYNOTE-689 and NIVOPOSTOP provide new potential for Erbitux® in 1L R/M

ERBITUX CETUXIMAB

2026

The impact of the internal and external SCCHN environment on the new brand plan

KEY CHANGES VS. LAST YEAR

INTERNAL ENVIRONMENT

- **Growing RWE** in sequencing and **evidence** in 2L (PACE-ACE)
- **Q2W** registration
- Some **RWE** (CSS) **and ISS** with cetuximab were **initiated** (TATIANA, AVEC-119, ERBIOTAX, PREDINHANCE, TERENCE)

EXTERNAL ENVIRONMENT

- Growing experience with **ICI in R/M setting** including in 1L as aligned to KEYNOTE-B10
- No major changes in the R/M treatment landscape are expected although **KEYNOTE-689** and **NIVOPOSTOP** could impact the patient journey
- **Erbitux® & ICI biosimilars / bioequivalents** introduction to some markets

LOOKING BACK ON OUR BRAND PLAN…

SIs from last year

ENGAGE

Among all SI prioritise reinforcement positions in the 1L strengthening SoC image

EACH 1L PATIENT MATTERS!

- Highlight factors beyond CPS which should be taken into consideration when choosing 1L treatment
- Focus on RWE and QALY data
- Leverage Erbitux® 1L CPS-agnostic efficacy and flexible use
- Showcase patient profiles who can benefit from the Erbitux® choice in the 1L
- Scale HCPs positive experience of 1L treatment with Erbitux®

EXPAND

Go to **2L promotion only when 1L opportunities are used by maximum**

Consider **LA** as an **additional business source** rather than a core

Optimise DoT across the continuum of care

- Demonstrate 2L insufficient treatment rates and Erbitux® advantages vs CT
- Capitalise on efficacy data in LA in dedicated countries

ENHANCE

Continue to **explore LCM and evidence generation**

Medical Priorities

	SI 1: ENGAGE	SI 2: EXPAND	SI 3: ENHANCE
	Reinforce our core to grow	**Leverage opportunities to grow**	**Build future opportunities to grow**
Priorities	**REINFORCE Erbitux® positioning for all 1L R/M eligible patients**	**DEMONSTRATE optimal treatment strategy to reinforce use of Erbitux® across the continuum of care**	**CAPITALISE on Erbitux® regimen flexibility to support new growth opportunities**
Key tactics	• **Reinforce** that CPS is not the only criterion to select 1L treatment • **Strengthen** the role of personalised treatment and demonstrate benefits of 1L Erbitux® use in different R/M subpopulations • **Communicate** the importance of sequencing when selecting 1L treatment • **Generate** additional evidence, including RWE, on 1L Erbitux® use	• **Optimise** R/M SCCHN treatment sequencing e.g., through communication and evidence generation, including: ○ 2L Erbitux® (+/- CT) use following progression on 1L ICI regimens (including taxanes +/- Pt) ○ Importance of proactive planning and receiving both Erbitux® and ICI as part of the patient journey • **Drive** scientific advocacy for Erbitux® use in eligible LA patients	• **Leverage** current studies and evidence generation programs to demonstrate Merck's commitment to SCCHN, PAGs and HCPs • **Generate** evidence and increase awareness for Erbitux® CT-backbones and flexible use • **Support** new Erbitux® combinations by insight generation, leveraging evidence and communication

Dashboard Jul 2025 – SCCHN Market Insights

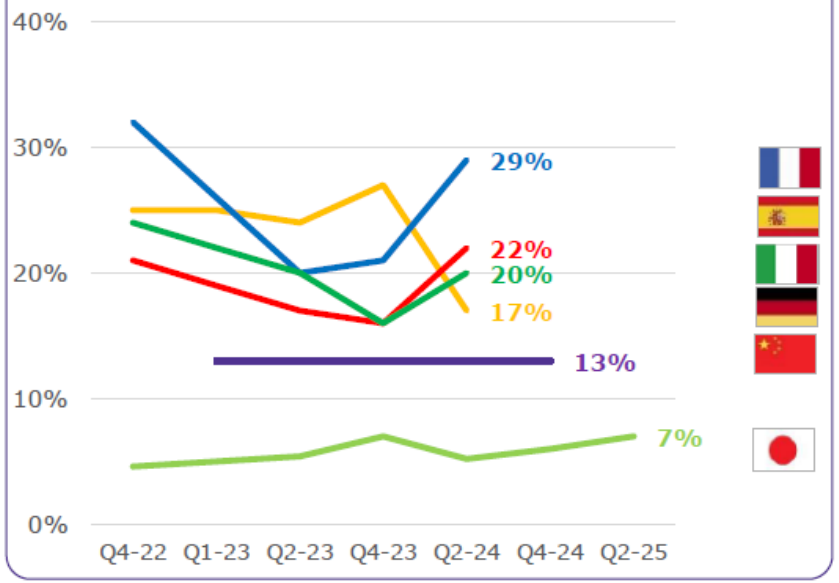
ERBITUX CETUXIMAB

Based on the latest data (EU4-Q4'24, 3xannual in 2022, 2 waves 2023 and 2024; Japan – H1'25 2 waves in 2023 and 2024, quarterly 2022; CN 2023 and 2024 customer insight study, annual data

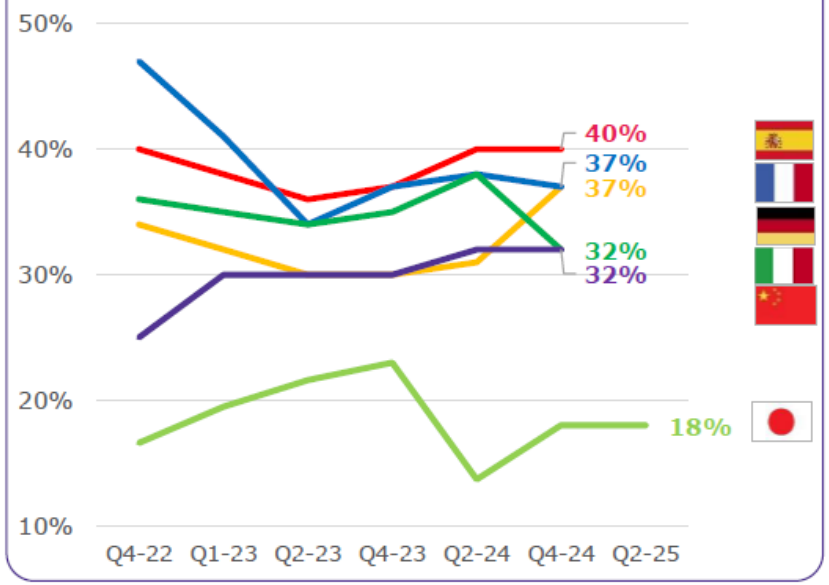
No new tracker readout in Jul

CN DE FR UK ES IT JP

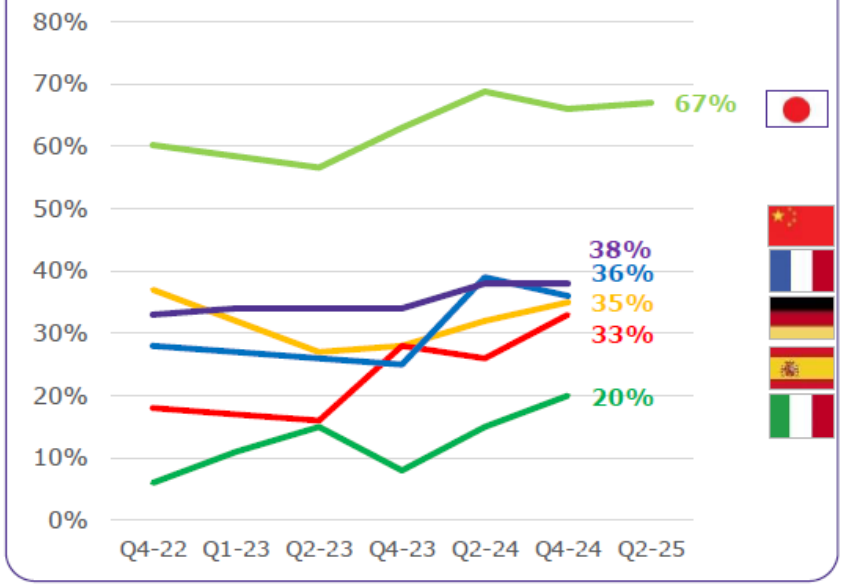
Erbitux pts share - LA SCCHN



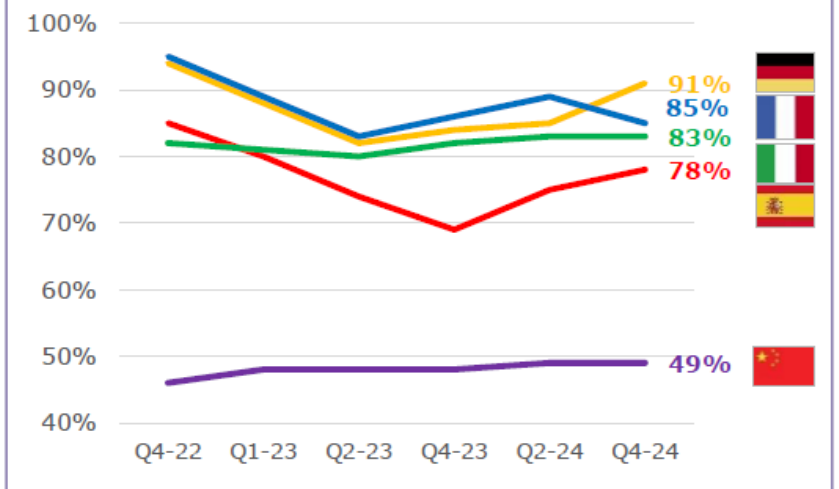
Erbitux pts share - 1L R/M



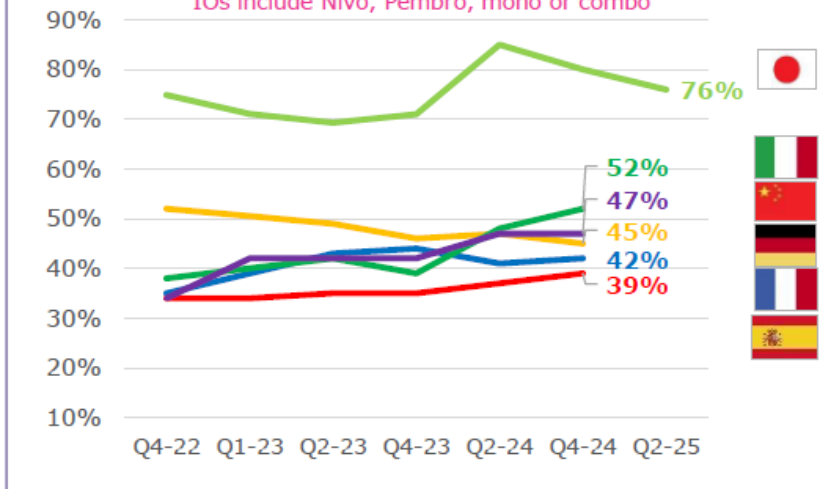
Erbitux pts share - 2L+ R/M



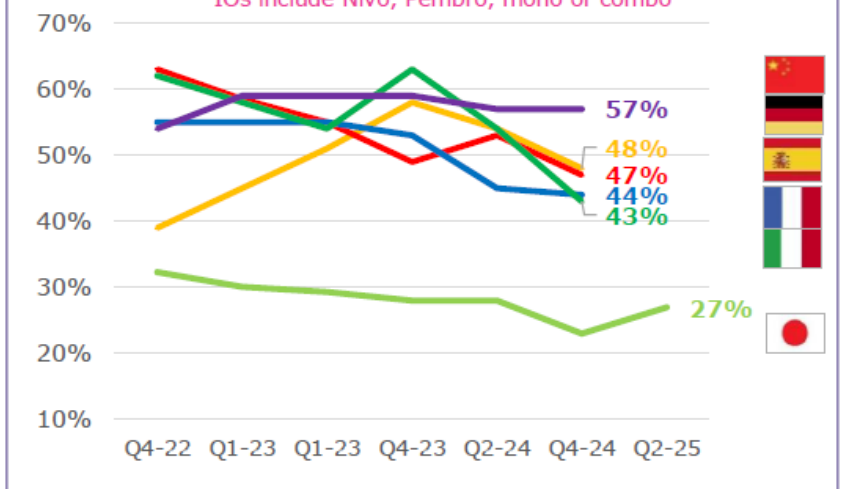
PD-L1 Testing Rate- 1L R/M



Total IOs pts shares - 1L R/M

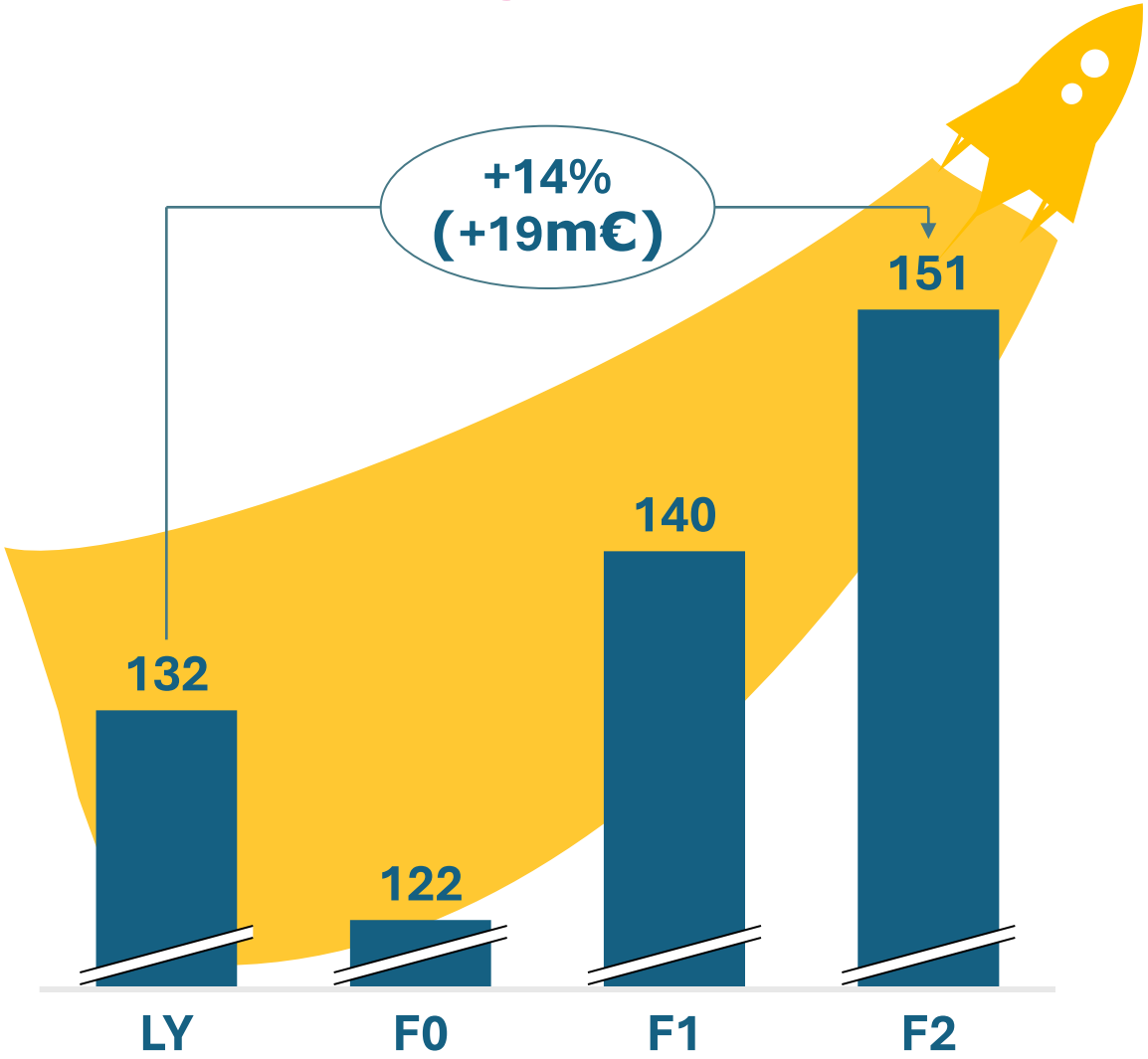


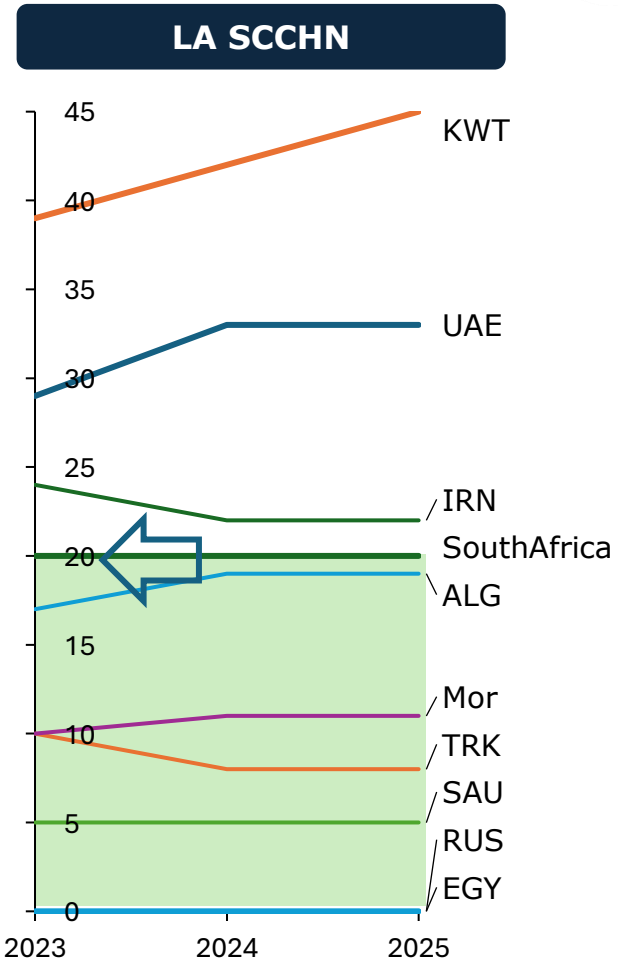
Total IOs pts share - 2L+ R/M

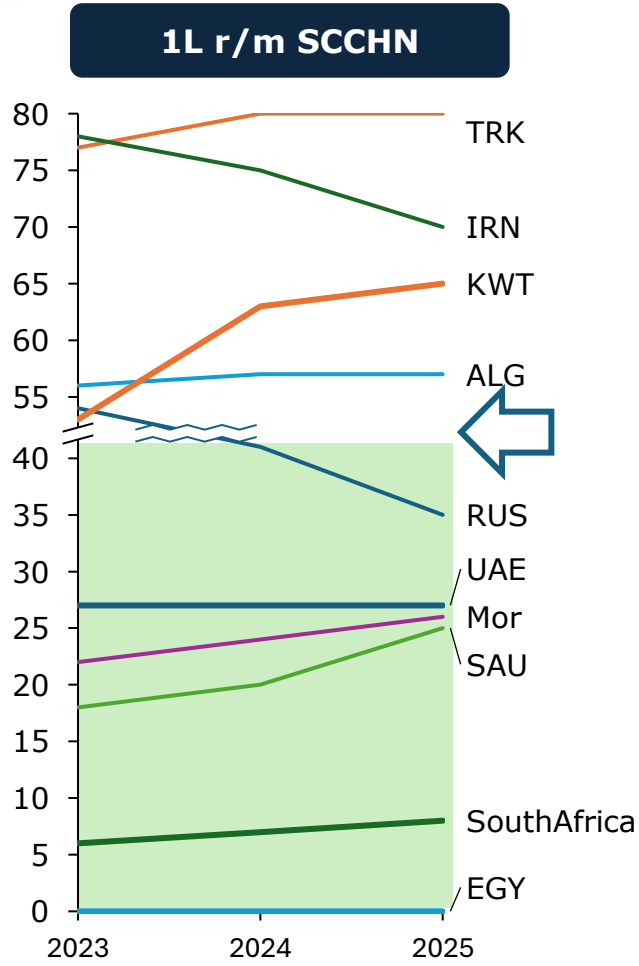


Source: EU4 SCCHN Tracker Cerner Enviza –2 waves annual data; JP SCCHN Tracker M3 2 waves annual data;China IQVIA SCCHN customer insight study

Erbitux MEAR
+24% gr vs LY YTD/8 inland sales







23 Sep'25

DAY 2

WE ARE UNSTOPPABLE
Reigniting Erbitux in MEAR

Go Beyond 2025

5 mins	Opening and objectives	*Mohamed and Harshveer*
10 mins	**What makes our teams unstoppable in Oncology?**	*GMs (Ahmed, Moncef & Haitham) and Alena*
SCCHN		
5 mins	Introduction…	*Harshveer and Pauline*
10 mins	· **My story!**	*Head and Neck Cancer fighter (video)*
5 mins	Q/A	*All*
15 mins	· **Strategies in management of head and neck cancer**	*Professor Thorsten Füreder*
10 mins	Q/A	*All*
10 mins	**Strategy and Performance: Erbitux in SCCHN**	*Andrey, Pauline, Mohamed and Niklas*
5 mins	**Panel discussion:**	*Moderator: Mohamed and Harshveer*
15 mins	· **Behavioral segmentation and Messaging**	*Panel: Barbara, Andrey, Pauline,*
10 mins	· **How to raise the bar in execution in SCCHN?**	*TRK, NA and NE*
	Q/A	*All*
10 mins	**Coffee break**	
CRC		
10 mins	**Strategy and Performance: Erbitux in CRC**	*Mohamed, Filippo and Niklas*
15 mins	**Panel discussion:**	*Moderator: Mohamed and Harshveer*
	How to raise the bar in differentiation in CRC 1L LS RAS wt ?	*Panel: Barbara, Filippo,*
10 mins	Q/A	*RUS, KSA, NA*
		All
5 mins	**Breakout room #1(RUS,IR,TRK)**	*Moderator: Patricia*
	Differentiation vs NCB	*Panel: Barbara, Harshveer, Ihab & Patricia.*
15 mins	**Introduction …**	
	Panel discussion	*Country BUH, Med., Reg. and MAP*
	Q/A	
	Breakout room #2 (rest of MEAR)	*Moderator: Mohamed and Filippo*
	Reviving Rechallenge	*Country: MKTG and Medical*
	Introduction …	
	Panel discussion	
	Q/A	
10 mins	**Insights from the 2 groups:** Group lead	
	Closing day 2	

R/M SCCHN segmentation guidance

! Segmentation guidance should be adapted based on country market situation and priorities with a main criteria to provide relevant messaging to existing segments !

	Erbitux® Convinced	Rational Thinker	ICI Strategist	ICI Enthusiast
Preferred 1L treatment	**Erbitux® + CT***	**Erbitux®- or pembrolizumab-based regimens**	**Pembrolizumab-based regimens**	**Pembrolizumab-based regimens**
Clinical behaviour	• Values Erbitux® for its enduring efficacy and long-term experience • **Considers Erbitux® + CT* as the first choice** in 1L for most patients • Only considers pembrolizumab ± platinum + 5-FU for **patients with high CPS (CPS≥20) or in 2L**	• Considers the individual patient's needs • Considers CPS as not the only factor of treatment choice • Symptoms relief, need of high response or tolerability are factors taken into consideration while choosing the treatment	• **Strongly believes in the results of KEYNOTE-048** • Passionate about ICIs and uses pembrolizumab-based regimens in 1L • Considers Erbitux® -based therapy in 1L for patients with CPS<1 or contraindicated to ICI • **Uses Erbitux® -based therapy in 2L**	• **Strongly believes in the results of KEYNOTE-048** • Passionate about ICIs and uses pembrolizumab-based regimens in 1L • Only considers Erbitux® -based therapy in 1L for patients with CPS<1 or contraindicated to ICI • **Doesn't use Erbitux® -based therapy in 2L**
Messaging strategy	• Reinforce the **rationale** for the use of **Erbitux® + CT* in 1L**	• Leverage RWE and QALY study data to demonstrate that **different treatment sequences can be beneficial for CPS 1-19** patients and **factors beyond CPS** should be taken into consideration while choosing 1L treatment • Focus on **patient profiles with CPS 1-19 and frail patients** for whom **1L Erbitux® + CT*** is a reasonable choice • Communicate the efficacy results for 1L Erbitux® + CT* that occur **independently of CPS**, and highlight the **flexibility** of the Erbitux® + CT* regimen • Communicate the **response rates of 1L Erbitux® + CT***	• Reinforce efficacy of **1L ICI followed by 2L Erbitux® + CT*** sequence	• Discuss the **importance of considering treatment sequence** early • Highlight the efficacy of **1L ICI followed by 2L Erbitux® + CT*** sequence
SIs	Strengthen Erbitux® SoC image as an efficacious choice for 1L R/M SCCHN patients			
	Optimise DoT across the continuum of care			
Content			Increase 2L Erbitux® usage in all 1L Erbitux® untreated patients	
	1L master-deck		2L master-deck	

* Platinum-based chemotherapy

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10 mins	Q/A	*All*
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10 mins	**Insights from the 2 groups:** Group lead Closing day 2	

‘Pioneering Backbone’ Communication (1/2)

Erbitux® is pioneering anti-EGFR therapies as the backbone treatment for mCRC *RAS* wt patients, with its significant survival benefits, high response rates, trusted experience and innovation[1–29]

Erbitux® was the **FIRST approved anti-EGFR therapy** in mCRC and paved the way for precision medicine in *RAS* wt mCRC[12]

Erbitux® was the:

- **FIRST to deliver** pivotal data demonstrating the **benefit of anti-EGFR therapies** in mCRC [BOND][2]
- **FIRST to highlight** their advantages in **1L treatment settings vs CT** [CRYSTAL][3]
- **FIRST to show benefit over bevacizumab-based regimens** [FIRE-3][13]
- **FIRST to demonstrate the importance of primary tumour-sidedness** [NCIC CO.17 and CALGB/SWOG 80405][6,7]

Erbitux® has become the **FIRST anti-EGFR** to offer a new therapy option for patients with ***BRAF* V600E mt mCRC**[14,15]

- It has become **SoC in 2L** as part of the BEACON regimen[16,17]
- Based on BREAKWATER, it is expected to become the **new SoC in 1L***[18]

*Approvals vary by market. 1L, first-line; 2L, second-line; CT, chemotherapy; EGFR, epidermal growth factor receptor; SoC, standard of care.

1. EMA. 2004. Available at: https://www.ema.europa.eu/en/documents/scientific-discussion/erbitux-epar-scientific-discussion_en.pdf (last accessed May 2025); 2. Cunningham D, et al. N Engl J Med 2004;351:337–345; 3. Van Cutsem E, et al. N Engl J Med 2009;360:1408–1417; 4. Heinemann V, et al. Br J Cancer 2021;124:587–594; 5. Brulé S, et al. Eur J Cancer 2015;51:1405–1414; 6. Venook A, et al. J Clin Oncol 2016;34:suppl_abstr 3504; 7. BRAFTOVI SmPC. February 2023; 8. Pfizer Braftovi press release. 2025. Available at https://www.pfizer.com/news/press-release/press-release-detail/pfizers-braftovir-combination-regimen-significantly (last accessed May 2025); 9. Kopetz S, et al. New Engl J Med 2019;381:1632–1643; 10. ESMO Metastatic Colorectal Cancer Living Guidelines, v1.2 September 2024;11. Kopetz S, et al. Nature Medicine 2025; doi.10.1038/s41591-024-0344303; 12. Qin S, et al. J Clin Oncol 2018;36:3031 3039; 13. Arnold D, et al. Ann Oncol 2017;28:1713–1729; 14.Sobrero AF, et al. J Clin Oncol 2008;26:2311–2319; 15.Maughan T, et al. Lancet 2011;377:2103–2114; 16. Venook A, et al. JAMA 2017;317:2392–2401; 17.Chibaudel B, et al. ASCO 2022 (Abstract No. 3504 – presentation); 18. Pinto C, et al. J Clin Oncol 2024;42:1278–1287; 19.Merck data on file, 2024; 20. Petrelli F, et al. Oncology 2018;94:191–199; 21. Erbitux® EU SmPC, December 2024; 22. Bokemeyer C, et al. Future Oncol 2024;20:393–407; 23. Kasi PM. Oncologist 2022;27:336–337; 24. Vectibix SmPC, July 2022; 25. Tabernero J, et al. J Clin Oncol 2021;39:273–284; 26. Van Cutsem E, et al. J Clin Oncol. 2023;41:2628–2637; 27. Yaeger R, et al. New Engl J Med 2023;388(1):44–54; 28. Clinicaltrials.gov (last accessed May 2025); 29.Chictr.org (last accessed May 2025).

‘Pioneering Backbone’ Communication (2/2)

Significant survival benefit

Erbitux® + CT has demonstrated significant survival benefit vs both CT alone[1] and vs bevacizumab + CT in *RAS* wt mCRC, particularly in LS *RAS* wt mCRC[2,3]

- vs CT: TAILOR: 20.7 vs 17.8 months (p=0.02)[1]
- vs bevacizumab + CT:
  - FIRE-3: **38.2 vs 28.2 months (p=0.01)**[3]
  - CALGB/SWOG 80405: **39.3 vs 32.6 months (p=0.05)**[2]
- Phase III clinical trials in mCRC reporting mature OS data:
  - EPIC[4]
  - CRYSTAL[5]
  - COIN[6]
  - FIRE-3[3]
  - CALGB/SWOG 80405[7]
  - TAILOR[1]
  - STRATEGIC-1[8]
  - ERMES[9]

High response rates

Erbitux® + CT has consistently demonstrated high response rates in clinical trials, particularly in LS *RAS* wt mCRC[2,3,8]

- FIRE-3: **79%** (vs 68% for bev + FOLFIRI)[3]
- CALGB/SWOG 80405: **69.4%** (vs 57.9% for bev + FOLFOX/FOLFIRI)[2]
- STRATEGIC-1: 82.4% (vs 69.7% for bev + FOLFIRI) *RAS* wt/*BRAF* wt[8]

Erbitux® is pioneering anti-EGFR therapies as the backbone treatment for mCRC *RAS* wt patients, with its….

Innovation

Erbitux® continues to be studied in innovative combinations and settings, with several studies into novel combinations completed in recent years,[10–12,16] and over 270 planned or ongoing studies[17,18]

Novel combinations, studies in recent years:

- Erbitux® + encorafenib ± binimetinib[10–12]
- Erbitux® + encorafenib + CT[13]
- Erbitux® + adagrasib[16]

Erbitux® is the FIRST and only anti-EGFR to offer weekly or biweekly dosing alongside multiple CT options, setting the standard in empowering personalised and shared treatment decisions[19–22]

Trusted experience

High levels of experience have been built with Erbitux®, it has been studied in nine Phase III clinical trials in mCRC,[1,3,–9,13] is available in 116 countries,[14] and has been used to treat over 1.5 million patients[14]

Phase III trials in mCRC:*

- FIRE-3[3]
- EPIC[4]
- CALGB/SWOG 80405[7]
- CRYSTAL[5]
- TAILOR[1]
- STRATEGIC-1[8]
- COIN[6]
- ERMES[9]
- NCIC CO.17[13]

Extensive experience with Erbitux® means that it has a well-characterized safety profile and treatment discontinuations are uncommon[15]

CT, chemotherapy; LS, left-sided.

2026+ strategy: navigating market dynamics with commitment, innovation, and leadership

Brand positioning in mCRC

Erbitux® is **pioneering anti-EGFR therapies as the backbone treatment** for mCRC RAS wt patients, with its **significant survival benefits**, **high response rates**, **trusted experience** and **innovation**

	SI 1: ENGAGE	SI 2: EXPAND	SI 3: ENHANCE
	Reinforce our core to grow	**Leverage opportunities to grow**	**Build future opportunities to grow**
Objectives	**Differentiate Erbitux®** as the anti-EGFR of choice in **1L LS** leveraging **wealth of OS data, trusted experience and innovation**	**Establish Erbitux®** as the **new SoC** in **1L *BRAF* mt** **Leverage Erbitux®** in **1L RS** when tumour shrinkage is the goal **Expand Erbitux®** use to all eligible patients according to different market dynamics and accounts (3L+, among chemo-only & beva users) Optimise DoT across the **continuum of care**	**Shape strategic LCM:** realise new combinations and explore new indications Contribute to making Merck a **principal player in oncology** Optimise pricing, reimbursement and access Prepare for **2L KRAS G12C mt***
KPIs	✓ Anti EGFR market share (>60% worldwide) ✓ Increased Erbitux® SOV ✓ Engagement with top global KTLs as specified in the GMA plan	✓ 1L *BRAF* mt >90% MS peak share ✓ Ensure medical launch excellence for 1L BRAF mt indication ✓ RS market share >25 % ✓ Rechallenge MS >15%; beva/chemo MS <15% ✓ >27w DoT in 1L LS ✓ Respect of ISS milestones for clinical studies fitting DoT optimisation strategy	✓ Respect of ISS milestones for pivotal clinical studies fitting LCM strategy ✓ Maintained blockbuster status ✓ Price trend in line with long-term forecasts ✓ Focused launch readiness delivered for 2L KRAS G12C mut setting*

Behavioral segmentation & tailored Messaging are key in Erbitux

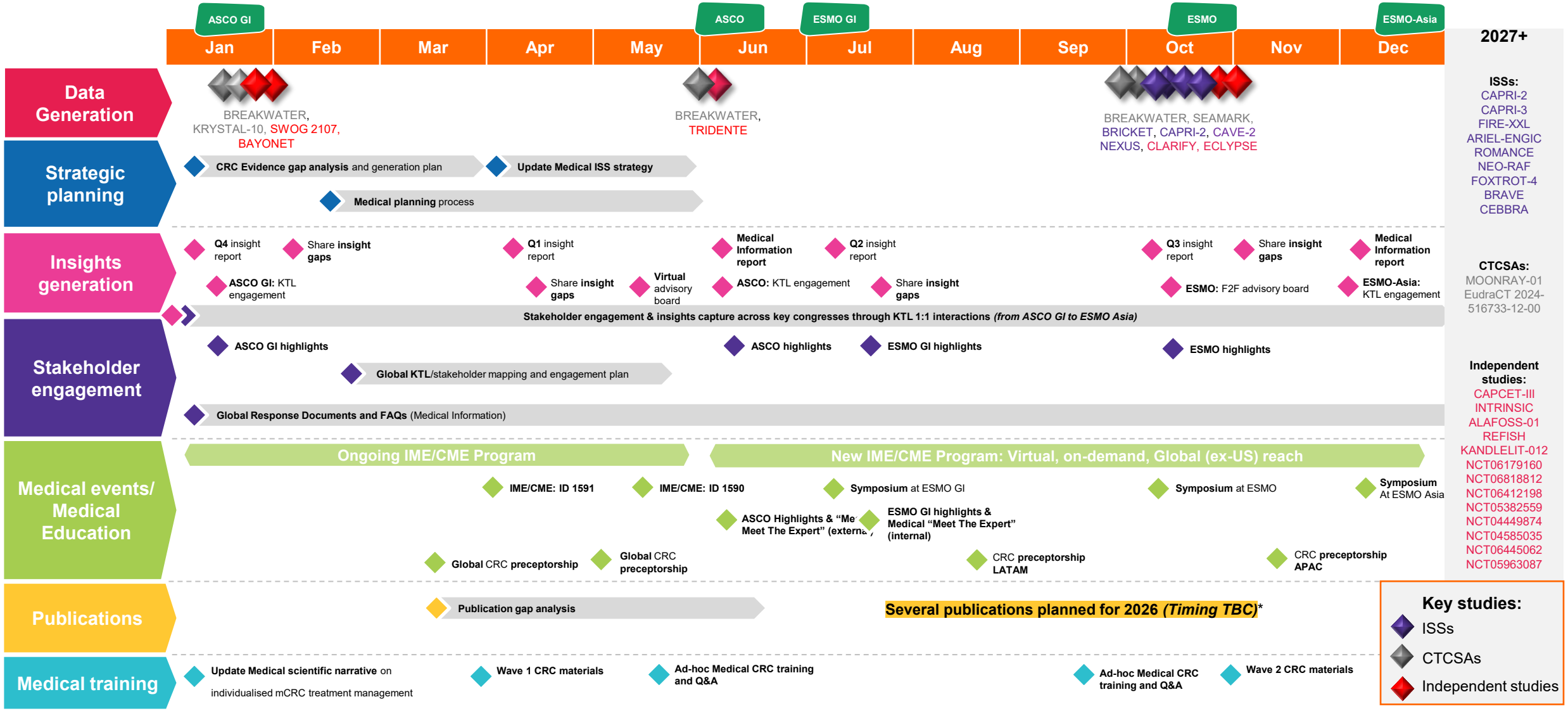
HCP segments	Patient segment				
	1L LS in anti-EGFR market	1L RS vs bevacizumab	DoT	Chemo-only Use in 1L LS	Rechallenge
Young User					
Mix User					
Erbitux® User					
Other Anti-EGFR User					
Beva User					
Chemo User					

Medical Priorities and tactics

	SI 1: ENGAGE	SI 2: EXPAND	SI 3: ENHANCE
	Reinforce our core to grow	**Leverage opportunities to grow**	**Build future opportunities to grow**
Priorities	**DRIVE personalised management and precision medicine to support clinical decision making in clearly defined patient subsets to expand the CoC**	**EMPHASISE optimal DoT across CoC through innovative treatment sequence strategies (maintenance, rechallenge, beyond PD), and BROADEN scientific reach of data to establish new SoC in 1L BRAF mt**	**PURSUE targeted LCM in new patient subsets (e.g., novel BRAF/KRAS mt settings) & PREPARE for Medical launches in strategic patient segments (e.g., KRAS G12C mt*)**
Key tactics	• **Generate and communicate** scientific evidence to differentiate Erbitux® vs other therapeutic strategies by emphasising anti-EGFR biomarker-driven tx approach • **Reinforce** importance of patient selection and increase HCP confidence in treating mCRC patients with Erbitux® • **Enhance** HCP engagement and education in mCRC to continue to build Merck's profile as a trusted partner in Oncology	• **Ensure** medical launch excellence for 1L Erbitux® with encorafenib & CT in BRAF V600E-mut patients through focused readiness and preparedness • **Support** data generation and dissemination on optimal treatment sequence, including maintenance strategies (de/re-escalation, stop & go), rechallenge, beyond PD • **Drive** HCP understanding and awareness of Erbitux's® key data to improve patient outcomes	• **Optimise** cetuximab LCM and support its positioning by generating, communicating, and disseminating evidence on novel cetuximab combinations and/or innovative therapeutic approaches for specific patient subsets (e.g., BRAF mt rechallenge, beyond PD, neo-adj, LLD, and KRAS G12X) • **Support** identification of new patient sub-groups through 3rd party collaborations • **Emphasise** Merck's scientific leadership and commitment to advancements in Oncology

Note: sub-headings may differ in the medical plan

Timeline for key Medical tactics

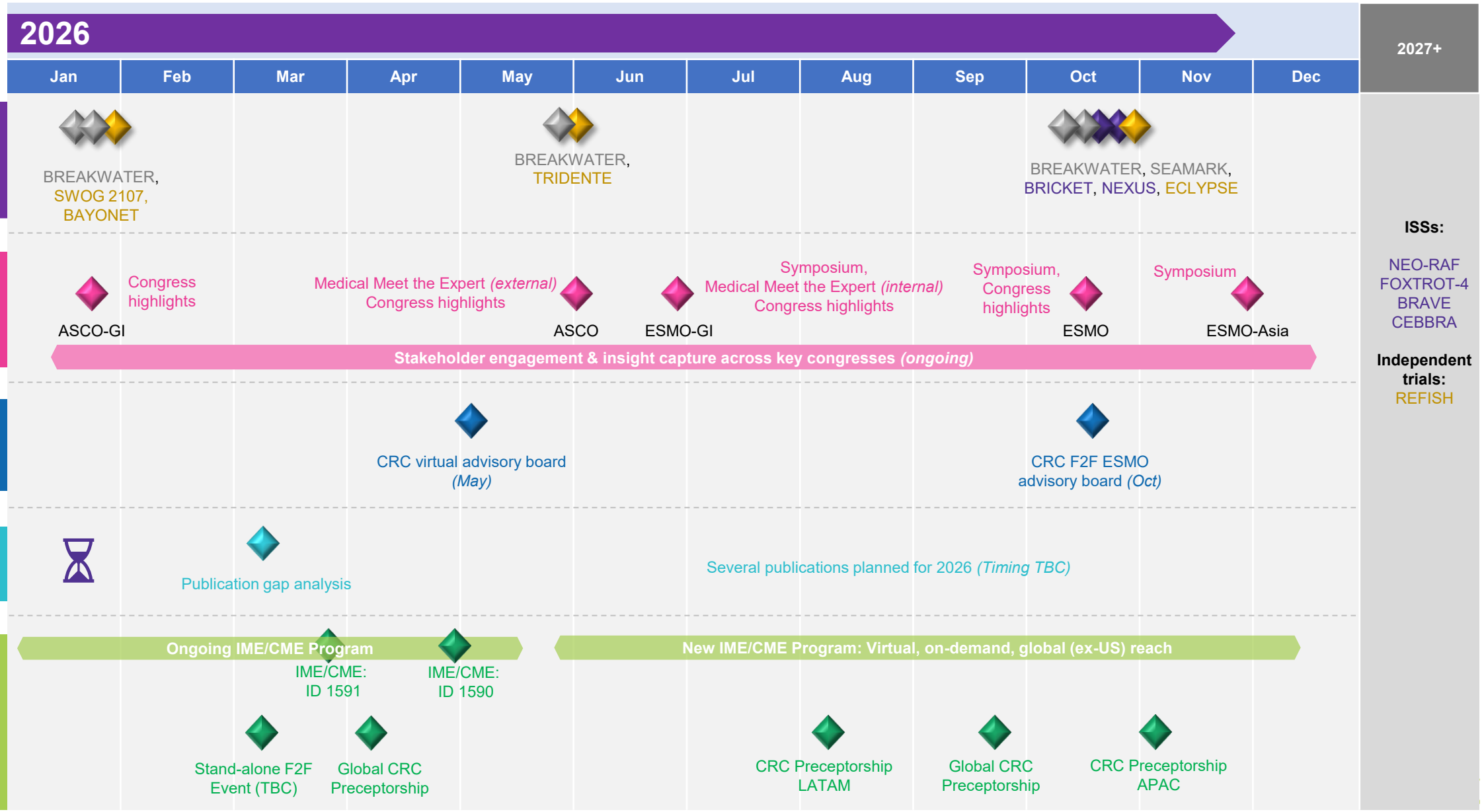


 For more details, please refer to detailed Med. Publications Plan

ERBITUX® CETUXIMAB

2026: Summary timeline of key events relevant to the 1L *BRAF* mt indication

Advisory boards | 3rd Party collaborations | Independent studies | Medical education events | ISSs | Congress & symposia



Dashboard Jul 2025 – mCRC Market Insights

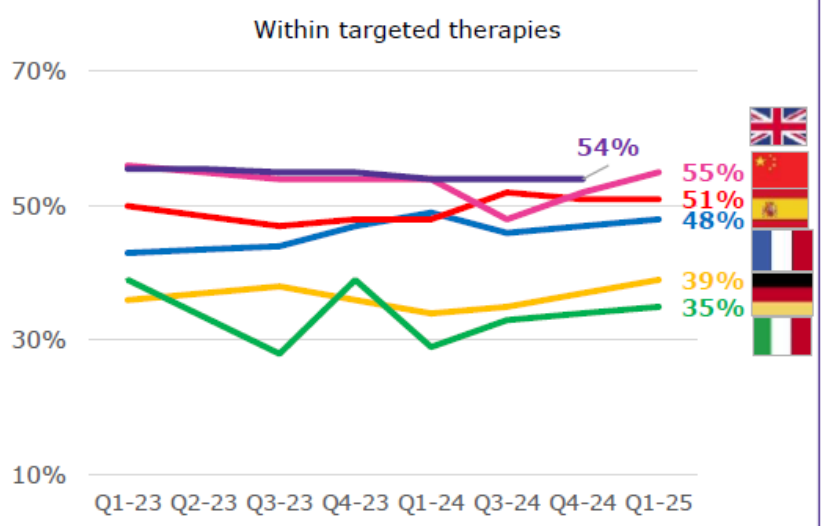
ERBITUX CETUXIMAB

Based on the latest data (EU5 to wave1/Q1'25, 2 waves in 2022-24; JPN – Q2'25 (2024-25 only monitor mCRC LS) - 3 waves yearly, China to Q4'24 annual data)

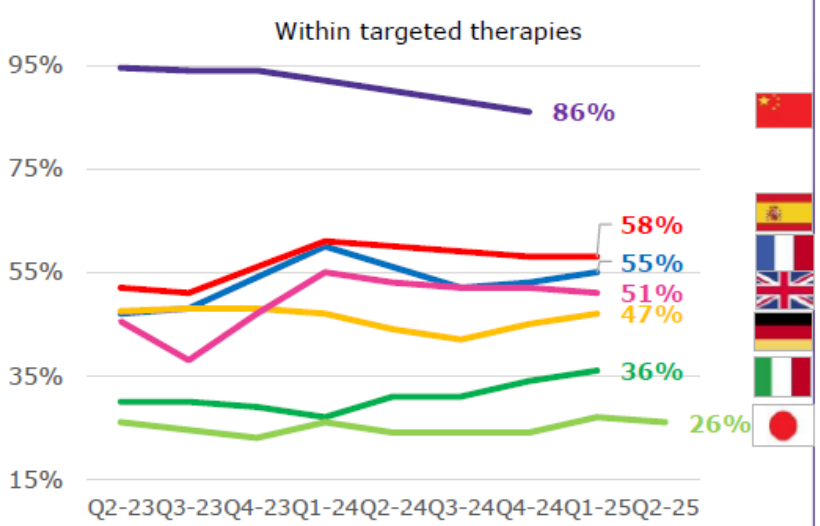
No new tracker readout in Jul

CN DE FR UK ES IT JP

Erbitux pts share of 1L mCRC RAS wt

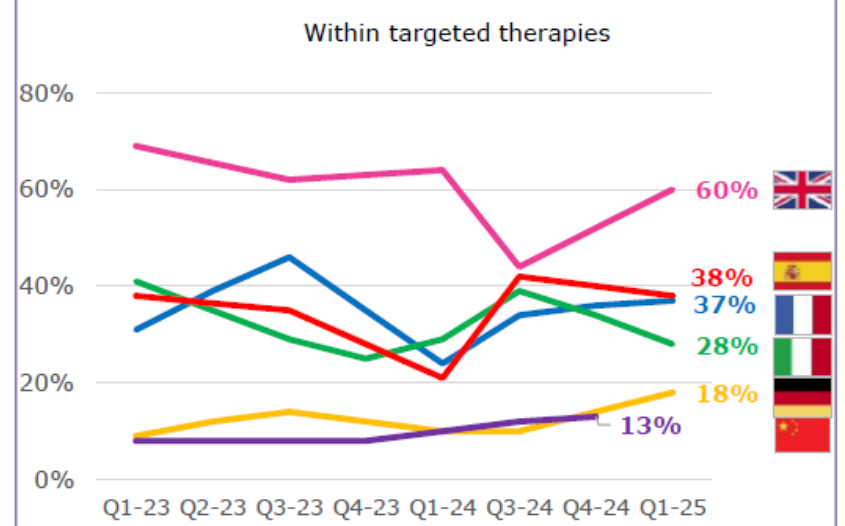


Erbitux pts share in Left side - 1L RAS wt



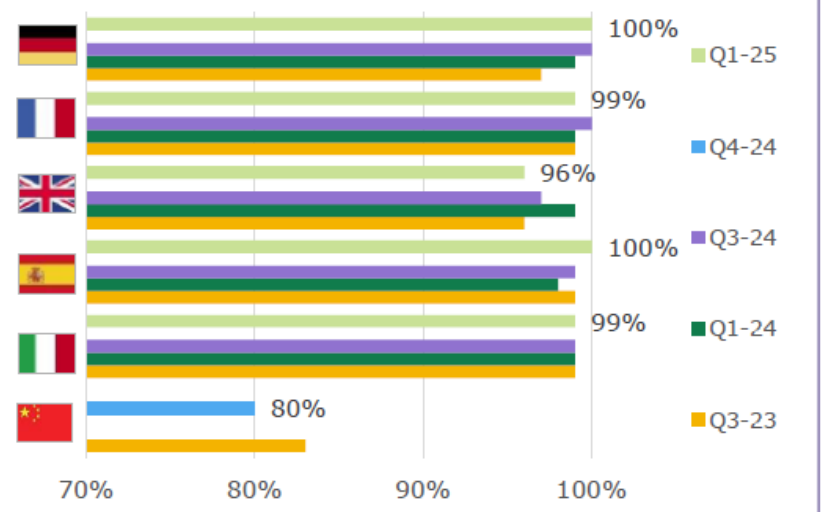
EU5 Rolling 6 months data

Erbitux pts share in Right side - 1L RAS wt



EU5 Rolling 6 months data

1L mCRC RAS Testing Rate

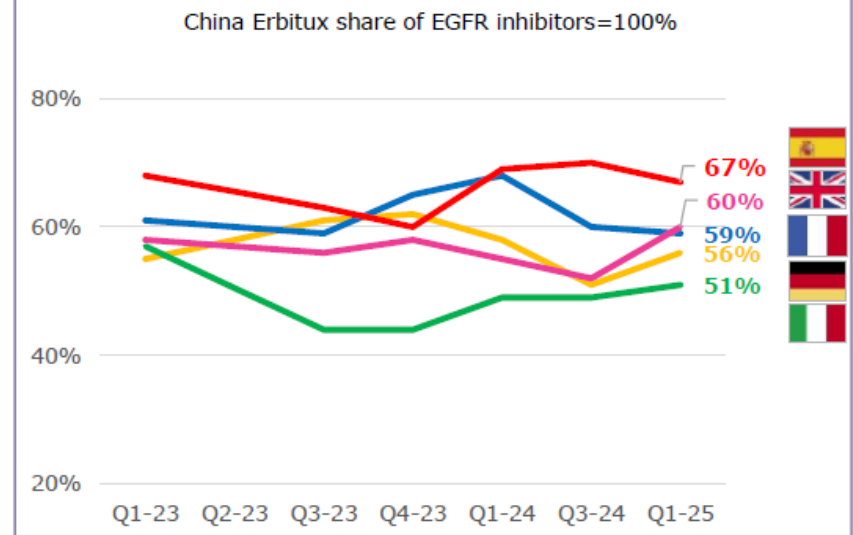


Erbitux 1L mCRC Treatment Duration (weeks)

Q1 25	30	25	26	32	30
Q3 24	29	24	27	30	27
Q1 24	26	24	26	29	28
Q3 23	31	27	30	39	31
Q1 23	28	25	28	28	22

*DoT for EU is based on MAT (moving annual total) data

EGFR share of 1L - Erbitux share vs Vectibix

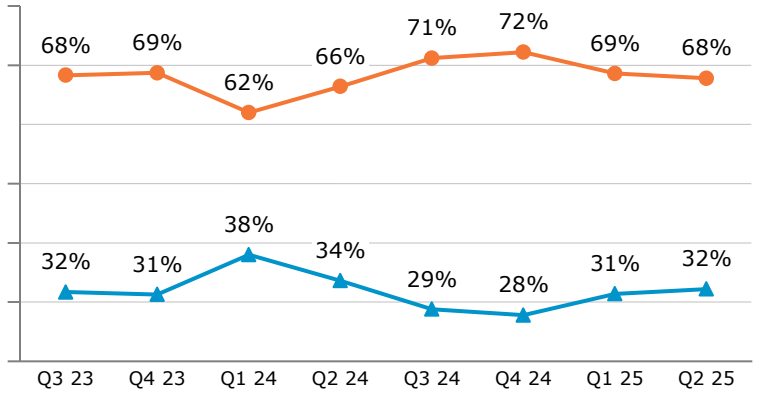


Source: EU mCRC Tracker IPSOS 2 waves/quarter since 2020, JP –mCRC M3 tracker; CN 1x annual

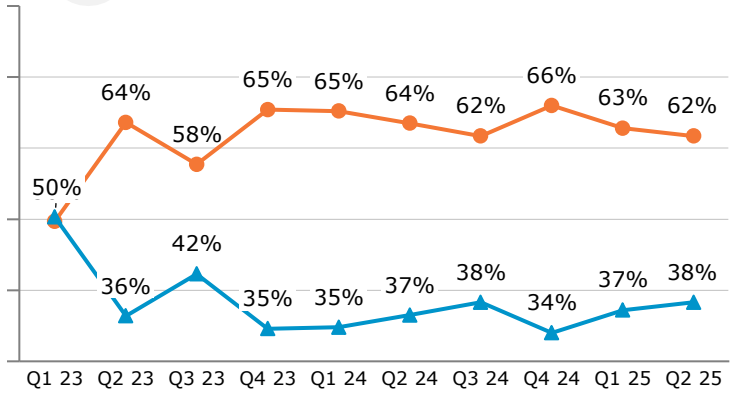
Erbitux remains the most used product in EGFR class with +60% or higher MS in majority of MEAR countries

Market Share — Erbitux — Vectibix/Panitumumab

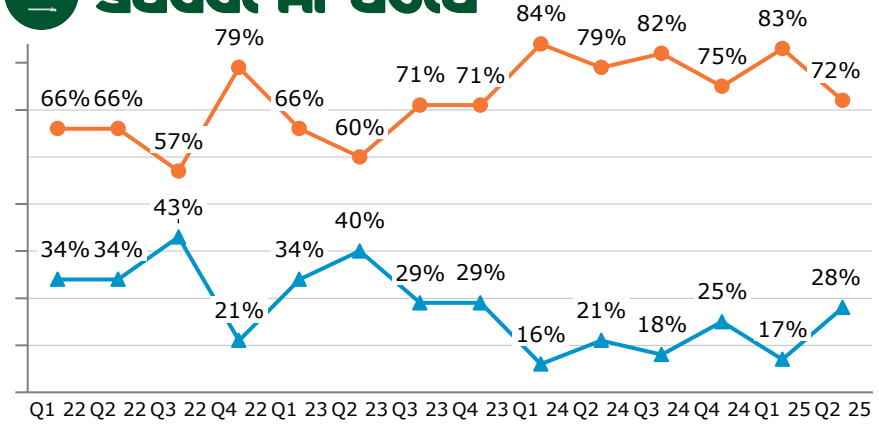
Russia



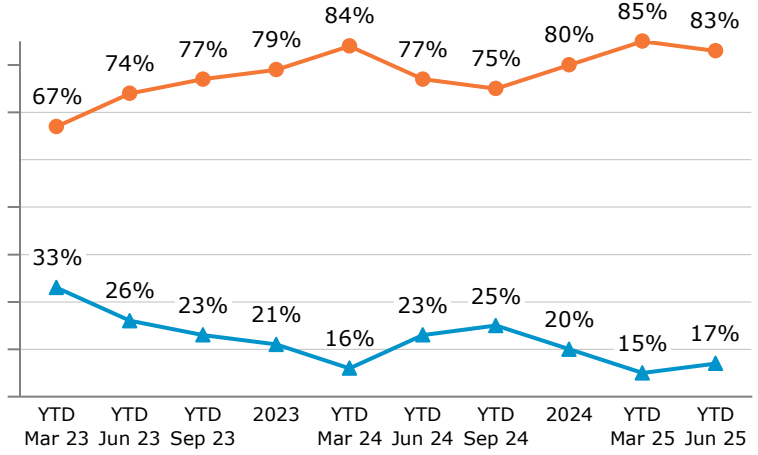
Turkey



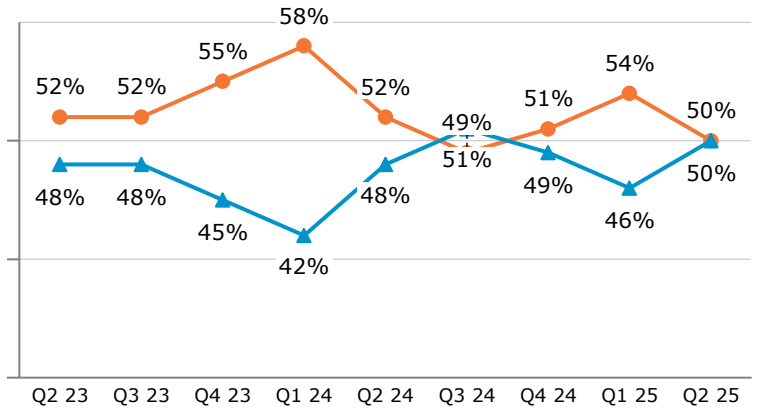
Saudi Arabia



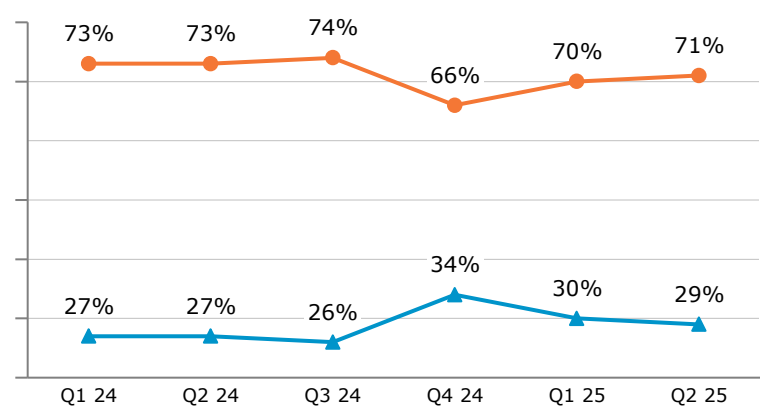
Gulf



Algeria



South Africa



Source: Country Teams
Units: Standard units

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Go Beyond 2025

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10 mins	**What makes our teams unstoppable in Oncology?**	*GMs (Ahmed, Moncef & Haitham) and Alena*
SCCHN		
5 mins	Introduction…	*Harshveer and Pauline*
10 mins	· **My story!**	*Head and Neck Cancer fighter (video)*
5 mins	Q/A	*All*
15 mins	· **Strategies in management of head and neck cancer**	*Professor Thorsten Füreder*
10 mins	Q/A	*All*
10 mins	**Strategy and Performance: Erbitux in SCCHN**	*Andrey, Pauline, Mohamed and Niklas*
5 mins	**Panel discussion:**	*Moderator: Mohamed and Harshveer*
15 mins	· **Behavioral segmentation and Messaging**	*Panel: Barbara, Andrey, Pauline, TRK, NA and NE*
10 mins	· **How to raise the bar in execution in SCCHN?**	*All*
	Q/A	
10 mins	**Coffee break**	
CRC		
10 mins	**Strategy and Performance: Erbitux in CRC**	*Mohamed, Filippo and Niklas*
15 mins	**Panel discussion:**	*Moderator: Mohamed and Harshveer*
10 mins	How to raise the bar in differentiation in CRC 1L LS RAS wt ?	*Panel: Barbara, Filippo, RUS, KSA, NA*
	Q/A	*All*
5 mins	**Breakout room #1(RUS,IR,TRK)**	*Moderator: Patricia*
15 mins	**Differentiation vs NCB**	*Panel: Barbara, Harshveer, Ihab & Patricia.*
	Introduction …	*Country BUH, Med., Reg. and MAP*
	Panel discussion	
	Q/A	
	Breakout room #2 (rest of MEAR)	*Moderator: Mohamed and Filippo*
	Reviving Rechallenge	*Country: MKTG and Medical*
	Introduction …	
	Panel discussion	
	Q/A	
10 mins	**Insights from the 2 groups:** Group lead	
	Closing day 2	

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Differentiation VS BGX/NCBs

Activities performed YTD	
RA	
Medical	
MAP	
Commercial	
Communication	
Legal	
Cross-Functional	

Planned Upcoming Activities			
Function	Activity	Lead	Timeline
RA			
Medical			
MAP			
Commercial			
Communication			
Legal			
Cross-Functional			

23 Sep'25

DAY 2

WE ARE UNSTOPPABLE
Reigniting Erbitux in MEAR

Go Beyond 2025

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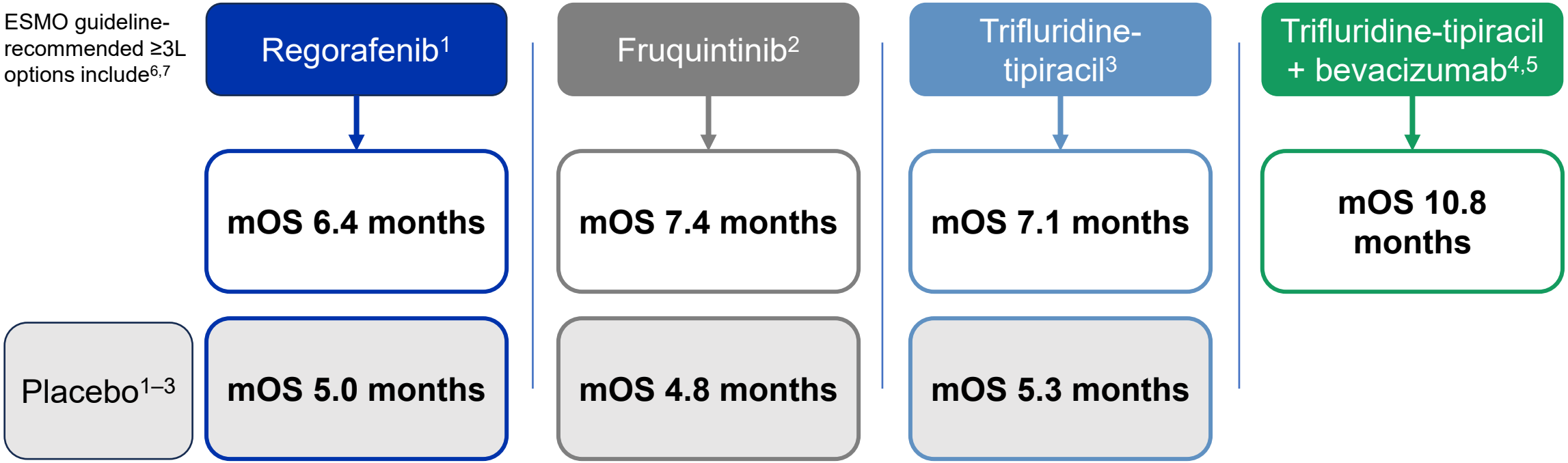
	Introduction …	
	Panel discussion	
	Q/A	
10 mins	**Insights from the 2 groups:** Group lead	
	Closing day 2	

Survival outcomes are poor for many of the guideline-recommended ≥3L treatments[1–6]

There is an **unmet need** for **effective treatments** that can prolong survival in 3L and beyond



Trial outcomes should not be cross-compared due to differing patient populations and study methodologies

3L, third-line; **ESMO**, European Society for Medical Oncology, **mOS**, median overall survival.

1. Grothey A, et al. Lancet 2013;381:303–312; 2. Dasari A, et al. Lancet 2023;402:41–53; 3. Mayer R, et al. N Engl J Med 2015;372:1909–1919; 4. Prager GW, et al. N Engl J Med 2023;388:1657–1667; 5. Tabernero J, et al. ASCO GI 2023 (Abstract No. 4 – oral presentation); 6. Cervantes A, et al. Ann Oncol 2023;34:10–32; 7. ESMO CRC living guidelines, v1.3 July 2025.

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Phase II and III trials have provided broad evidence to support anti-EGFR rechallenge as a ≥3L strategy[1–8]

Publication	Population	Study design	Patients (N)	ORR, (95% CI)	mOS, (95% CI)
Santini et al. 2012[1]	• *KRAS* wt* • Irinotecan-refractory, prior Erbitux® + irinotecan-based therapy benefit	Single-arm; **Erbitux® + irinotecan-based therapy** after ≥1 intervening LOT	39	**53.8% (39.1–63.7)**	Not reported
CRICKET[2]	• *RAS/BRAF* wt • Prior 1L Erbitux® + irinotecan-based therapy benefit, prior 2L oxaliplatin + bevacizumab-based therapy	Single-arm; **Erbitux® + irinotecan** as 3L treatment	28	**21.0% (10.0–40.0)**	**9.8 (5.2–13.10) months**
JACCRO CC-08[3]	• *KRAS* wt* • Prior 1L Erbitux®-containing therapy benefit	Single-arm; **Erbitux® + irinotecan-based therapy** as 3L treatment	34	**2.9% (0.07–15.3)**	**8.2 (6.1–11.7) months**
E-rechallenge[4]	• *RAS* wt • Refractory to standard therapies, prior benefit from Erbitux®	Single-arm; **Erbitux® + irinotecan** after ≥1 intervening CT line	33	**15.6%**	**8.6 months**
CITRIC[5]	• *RAS/BRAF/EGFR-ECD* wt • PD to 2L anti-EGFR free regimen	**Erbitux® + irinotecan** investigator's choice (excluding anti-EGFR agents)	66	**12.9% (3.6–29.8)** 0.0%	Not yet reported
FIRE-4[6]	• Previously untreated *RAS* wt mCRC	**Erbitux® + irinotecan/FOLFIRI** physician's choice (no anti-EGFR agents)	87	**26.7% (14.6–41.9)** 11.9% (4.0–25.6)	**17.6 months** 15.1 months
CHRONOS[7]	• *RAS/BRAF* wt • Prior response to anti-EGFR therapy, progression after anti-EGFR-free interval, ctDNA-confirmed *RAS/BRAF/EGFR-ECD* wt status at baseline	Single-arm; **panitumumab monotherapy**	27	**30.0% (12.0–47.0)**	**12.6 months**
PARERE[8]	• *RAS/BRAF* wt • Previously treated with a 1L anti-EGFR containing regimen, ≥1 intervening anti-EGFR free LOT	Arm A: **panitumumab** → regorafenib Arm B: regorafenib → **panitumumab**	213	ORR1: Arm A (**panitumumab**): **16.0%** Arm B (regorafenib): 1.9% ORR2: Arm A (regorafenib) 0.0% Arm B (**panitumumab**) **17.4%**	Not yet reported

Anti-EGFR rechallenge has consistently shown efficacy across **multiple Phase II[1–5,7] and III[6,8] trials**

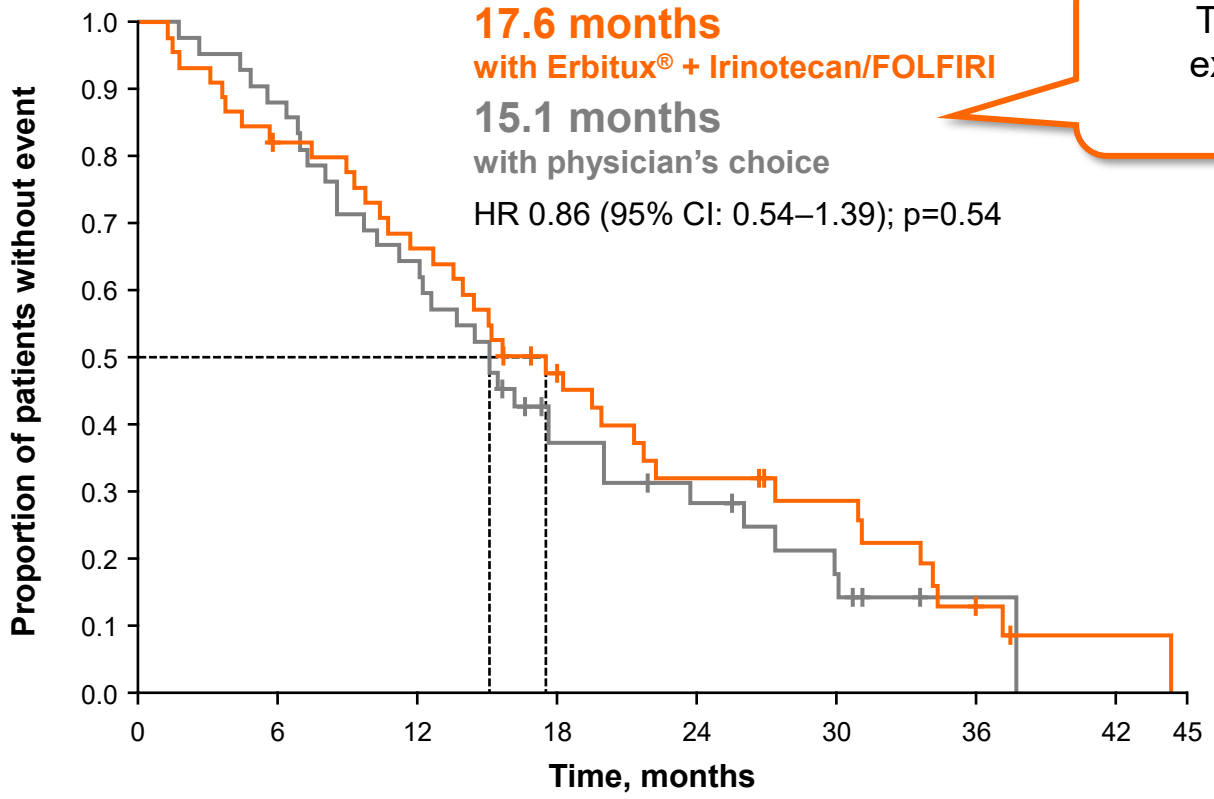
*Erbitux® is indicated for use in *RAS* wt mCRC; Erbitux® is not indicated for the treatment of patients with mCRC whose tumors have *RAS* mutations or for whom *RAS* mutation status is unknown.

1L, first-line; **2L**, second-line; **3L**, third-line; **CI**, confidence interval; **CT**, chemotherapy; **ctDNA**, circulating tumor DNA; **EGFR**, epidermal growth factor receptor; **HR**, hazard ratio; **LOT**, line of therapy; **ORR**, overall response rate; **ORR1**, first overall response rate; **ORR2**, second overall response rate; **mOS**, median overall survival; **PD**, progressive disease.

1. Santini D, et al. Ann Oncol 2012;23:2313–2318; 2. Cremolini C, et al. JAMA Oncol 2019;5:343–350; 3. Masuishi T, et al. Br J Cancer 2020;123:1490–1495; 4. Osawa H, et al. ESMO 2018 (Abstract No. 481P – poster presentation); 5. Santos Vivas C, et al. ESMO 2024 (Abstract No. 511MO – oral presentation); 6. Weiss L, et al. ASCO 2025 (Abstract No. 3513 – oral presentation); 7. Sartore-Bianchi A, et al. Nat Med 2022;28:1612–1618; 8. Cremolini C, et al. ASCO 2025 (Abstract No. LBA3515 – oral presentation).

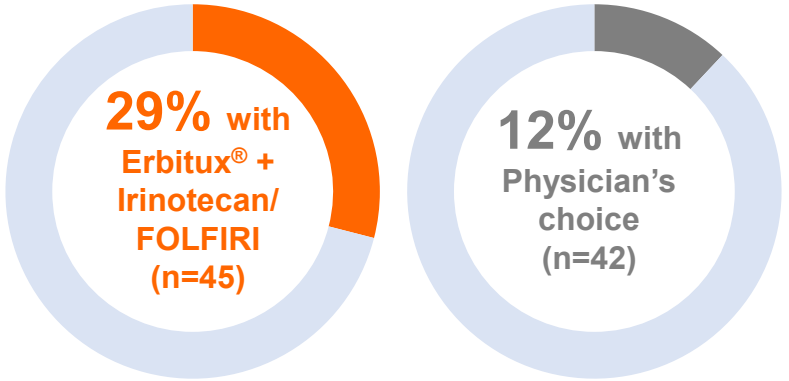
Anti-EGFR rechallenge led to mOS of 17.6 months in FIRE-4, and more than doubled response compared with physician's choice*[1]

OS (primary endpoint)



The control arm overperformed compared with expectations,[1] as many patients did not receive guideline-recommended treatments[1,2]

ORR



OR, 0.33 (95% CI, 0.11–1.04); p=0.07

*The FIRE-4 trial did not meet its primary endpoint of improved OS after R2.

3L, third-line; **CI**, confidence interval; **EGFR**, epidermal growth factor receptor; **ESMO**, European Society for Medical Oncology; **HR**, hazard ratio; **(m)OS**, (median) overall survival; **OR**, odds ratio; **ORR**, overall response rate; **R**, randomization.

1. Weiss L, et al. ASCO 2025 (Abstract No. 3513 – oral presentation); 2. ESMO CRC living guidelines v1.3 July 2025. Available at https://www.esmo.org/living-guidelines/esmo-metastatic-colorectal-cancer-living-guideline (last accessed July 2025).

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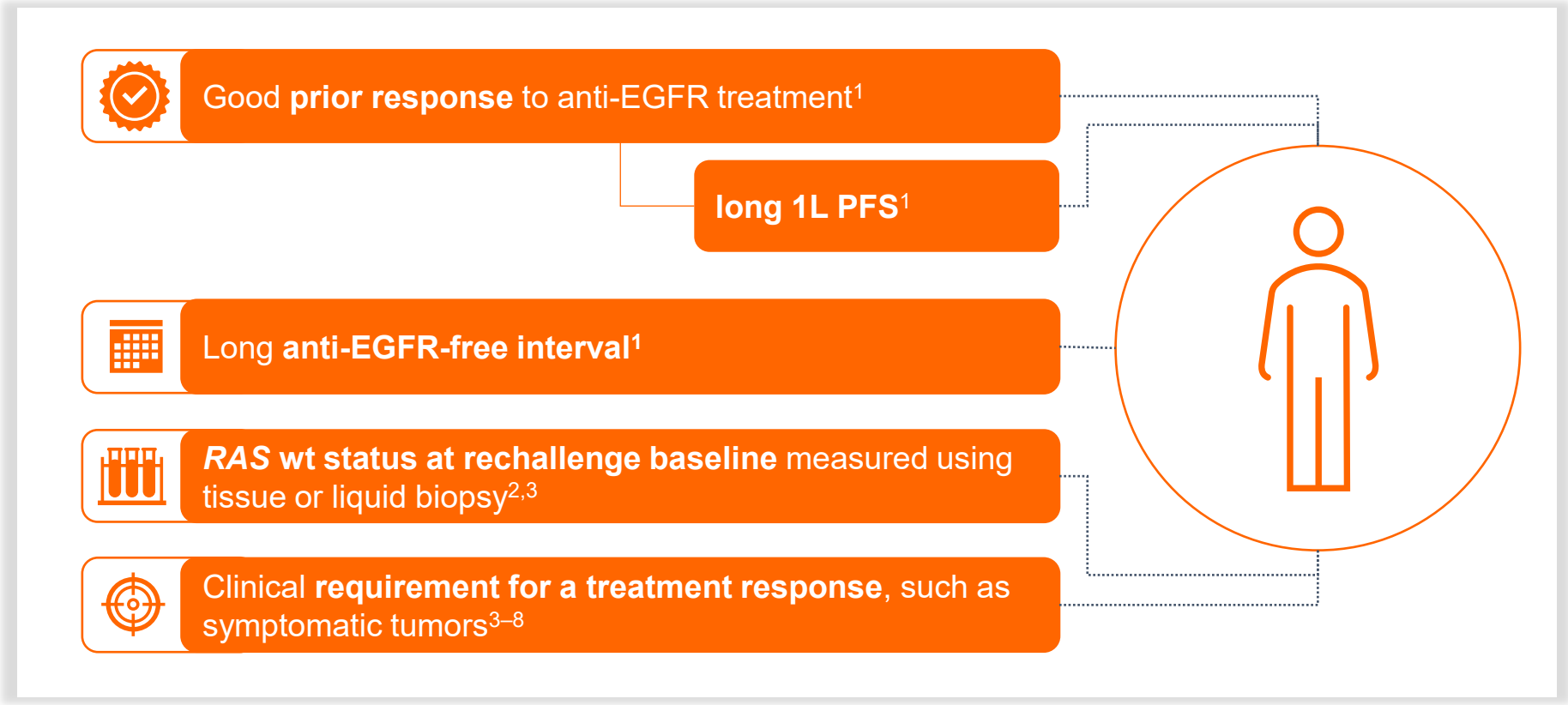
When should anti-EGFR rechallenge be considered?

There are several **patient and disease characteristics** which suggest that anti-EGFR rechallenge will be a potentially effective option for a patient[1–9]



1L, first-line; **EGFR**, epidermal growth factor receptor; **PFS**, progression-free survival.

1. Baselga PM, et al. ESMO GI 2025 (Abstract No. 42P – poster); 2. Pascual J, et al. Ann Oncol 2022;33:750–768; 3. Cremolini C, et al. JAMA Oncol 2019;5:343–350; 4. Santos Vivas C, et al. ESMO 2024 (Abstract No. 511MO – oral presentation); 5. Weiss L, et al. ASCO 2025 (Abstract No. 3513 – oral presentation); 6. Sartore-Bianchi A, et al. Nat Med 2022;28:1612–1618; 7. Cremolini C, et al. ASCO 2025 (Abstract No. LBA3515 – oral presentation); 8. Heinemann V, et al. Br J Cancer 2020;124:587–594;

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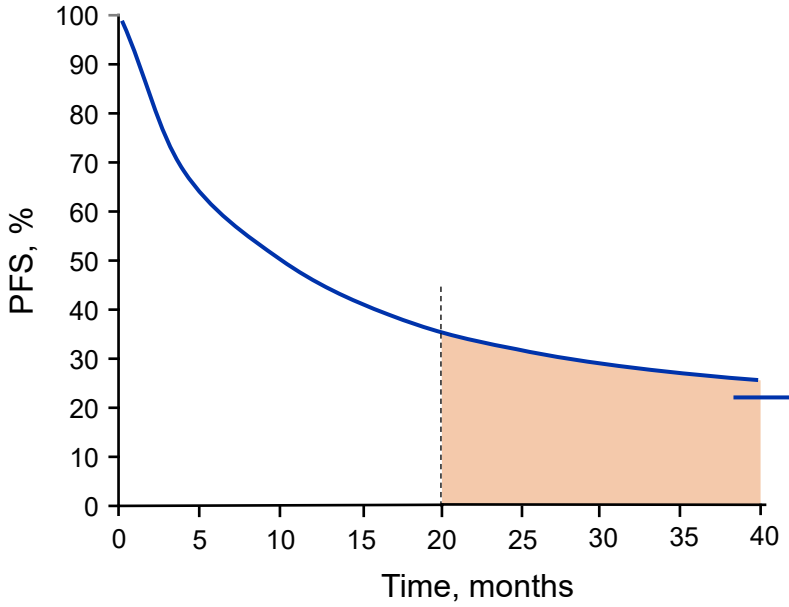
A long PFS on initial anti-EGFR therapy can predict favorable outcomes to rechallenge[1]

Real-world retrospective Spanish study[1]

Patients with *RAS* wt/*BRAF* wt mCRC treated with anti-EGFR rechallenge between 2018 and 2024 (N=134)

1L PFS on previous anti-EGFR therapy*



When receiving rechallenge, patients with PFS of more than 20 months on previous anti-EGFR therapy had:

Significantly longer PFS
(6.3 months vs 5.5 months; HR, 0.51; p=0.01)

Significantly higher DCR
(88% vs 62%; p=0.04)

Numerically longer OS
(16.3 months vs 14.2 months; HR not reported)

compared with PFS of less than 20 months

*Illustrative figure only – not representative of a real study.
CI, confidence interval; **DCR**, disease control rate; **EGFR**, epidermal growth factor receptor; **HR**, hazard ratio; **OS**, overall survival; **PFS**, progression-free survival.
1. Baselga PM, et al. ESMO GI 2025 (Abstract No. 42P – poster).

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Rechallenge messaging summary

One in three patients with mCRC survive to receive ≥3L therapy,[1] where there is an **unmet need for effective treatment options**

mOS of guideline-recommended 3L treatments*[2–6]

6–11 months

Anti-EGFR rechallenge is a **guideline-recommended strategy[6]** with a **strong scientific rationale** in *RAS* wt mCRC[7,8]

Recent data are defining the characteristics of patients who can **receive the greatest benefit** from anti-EGFR rechallenge[9–11]

- **Good prior response**
- **Long anti-EGFR-free interval**
- ***RAS* wt status at rechallenge baseline**
- **Requirement for a treatment response**

FIRE-4† has demonstrated a **long mOS** for Erbitux® + irinotecan/FOLFIRI rechallenge, supporting this approach in a **selected population**

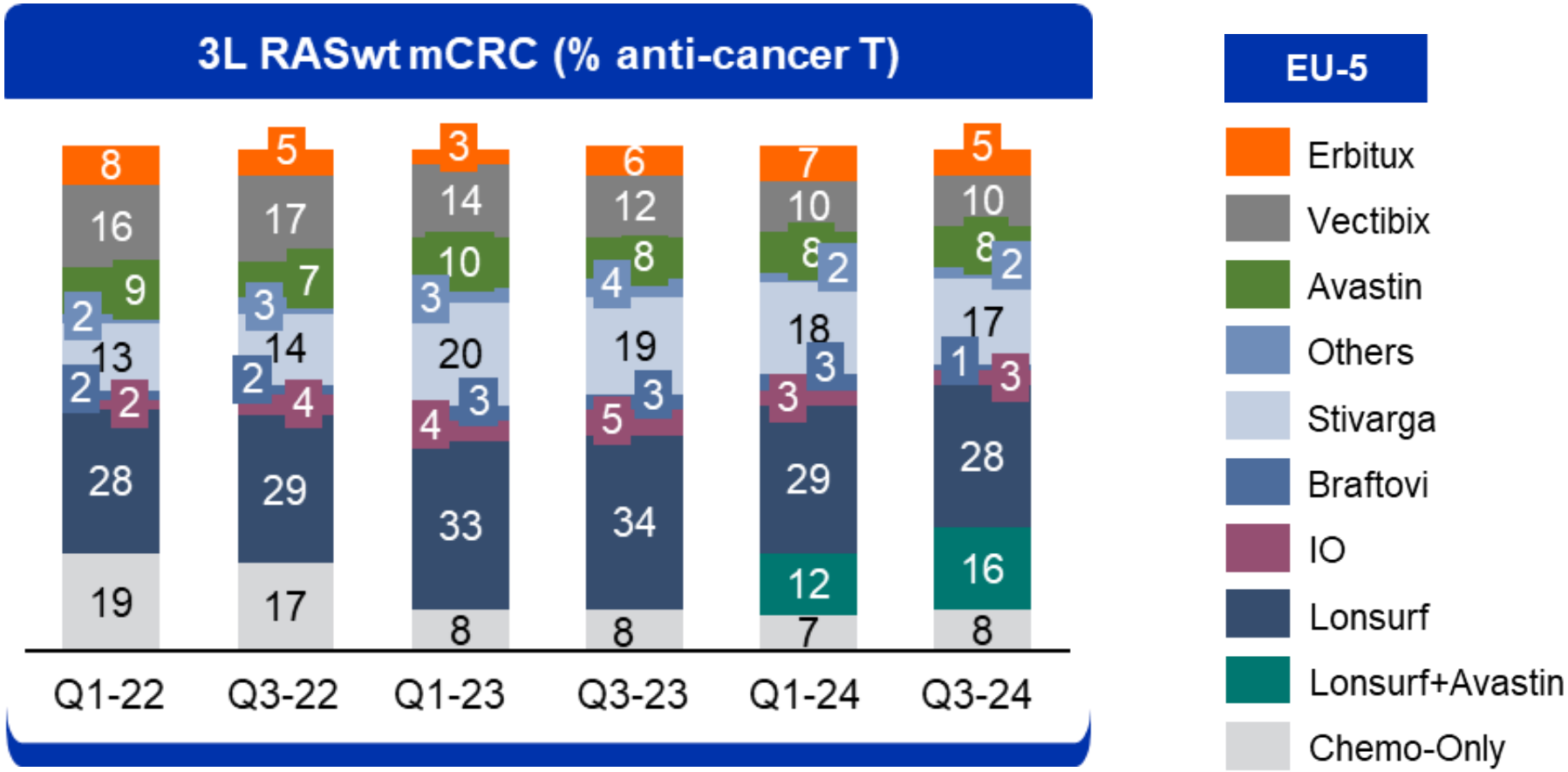
mOS of Erbitux® + irinotecan/ FOLFIRI rechallenge in **FIRE-4†**

17.6 months

*In Phase III clinical trials; †The FIRE-4 trial did not meet its primary endpoint of improved OS after R2.[12]
3L, third-line; **EGFR**, epidermal growth factor receptor; **(m)OS**, (median) overall survival; **R**, randomization.

1. Pericay C, et al. Cancers (Basel) 2023;15:4603. 2. Grothey A, et al. Lancet 2013;381:303–312; 3. Dasari A, et al. Lancet 2023;402:41–53; 4. Mayer R, et al. N Engl J Med 2015;372:1909–1919; 5. Prager GW, et al. N Engl J Med 2023;388:1657–1667; 6. ESMO mCRC living guidelines v1.3 July 2025. Available at https://www.esmo.org/living-guidelines/esmo-metastatic-colorectal-cancer-living-guideline (last accessed September 2025); 7. Santini D, et al. Ann Oncol 2012;23:2313–2318; 8. Parseghian CM, et al. Ann Oncol 2019;30:243–249; 9. Baselga PM, et al. ESMO GI 2025 (Abstract No. 42P – poster); 10. Cremolini C, et al. JAMA Oncol 2019;5:343–350; 11. Cremolini C, et al. Front Oncol 2023:12:946850; 12. Weiss L, et al. ASCO 2025 (Abstract No. 3513 – oral presentation).

Erbitux rechallenge current shares in EU



workshop discussions

1- what is the current reimbursement status of Erbitux rechallenge?
2- Erbitux rechallenge is 3L or 4L more?
3- Suggested actions to improve execution in Erbitux rechallenge ?