Cancers oeso-gastriques
Top 3 articles 2025

Khemara GNEP
Centre Armoricain de Radiothérapie, d'Imagerie et d'Oncologie
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Matterhorn

The NEW ENGLAND JOURNAL of MEDICINE

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Perioperative Durvalumab in Gastric and Gastroesophageal Junction Cancer

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MADRID 2023 ESMO congress 2025 ASCO BERLIN 2025 ESMO congress

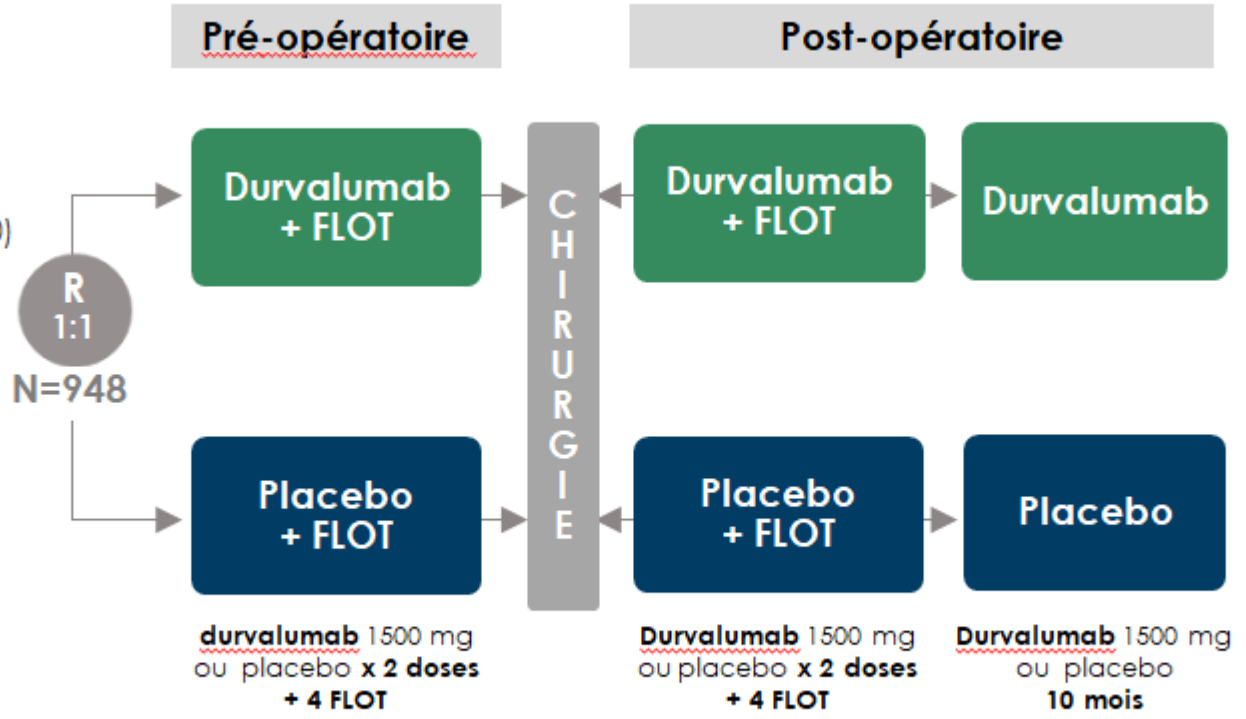
Matterhorn - Design

ADK gastrique ou JOG localisé

- Stade II, III et IV_A (>T2 N0-3 M0 ou T0-4 N+M0)
- M0
- Non prétraités
- ECOG PS 0 ou 1

Stratification

- Région géographique : Asie vs non-Asie
- N+ vs N-
- PD-L1 status : **TAP <1% vs TAP ≥1%**



Objectif principal :

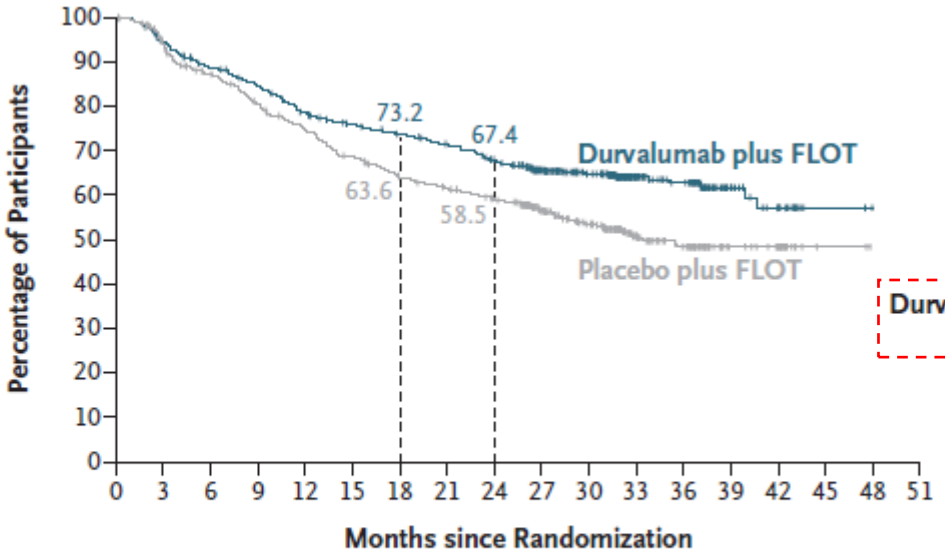
- Survie sans évènement (SSE)

Objectifs secondaires :

- Réponse histologique (revue centralisée : critères Ryan)
- SG

Janjigian, NEJM 2025

Matterhorn – EFS (CJP)



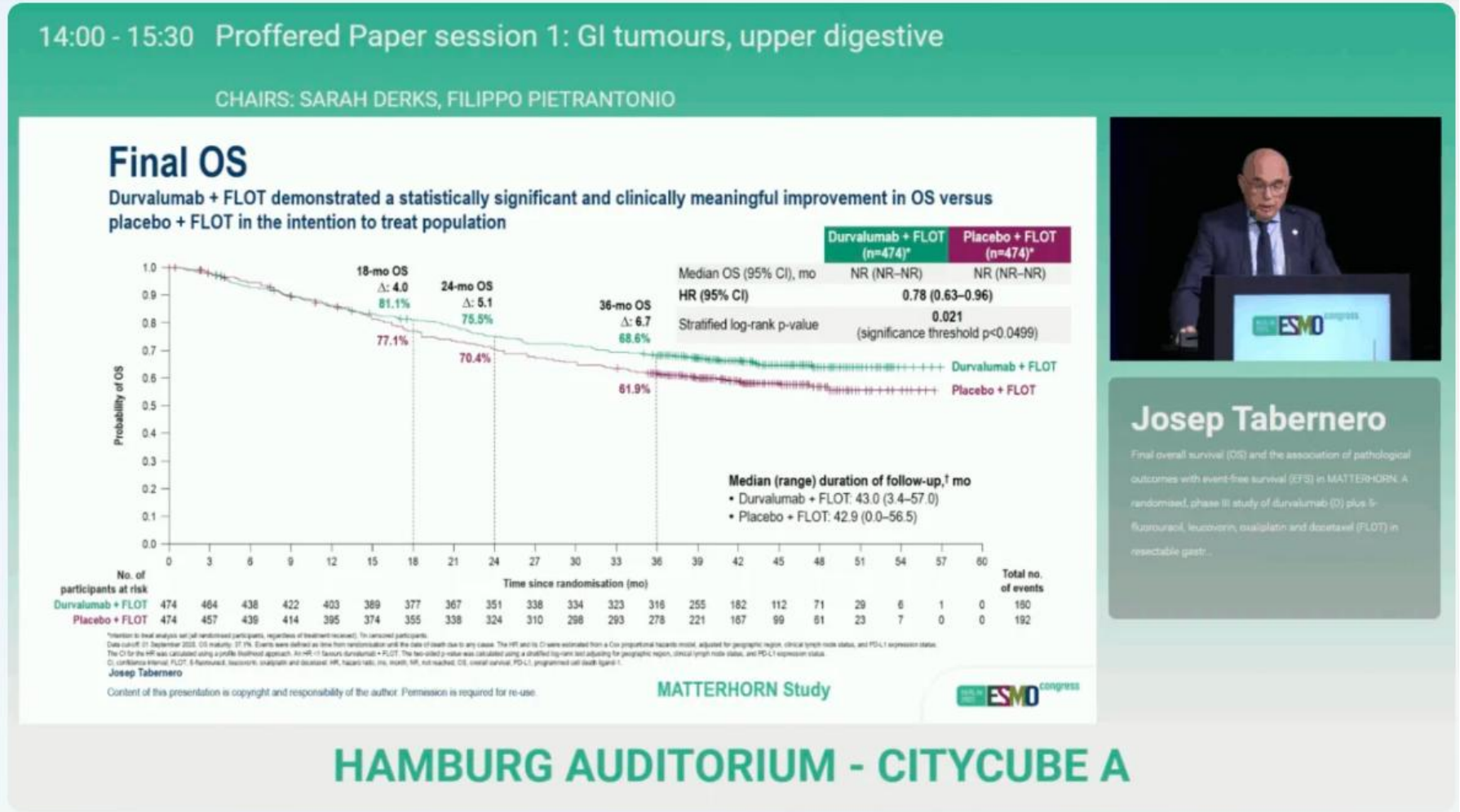
No. at Risk																		
Durvalumab plus FLOT	474	436	404	381	351	334	320	307	288	234	187	107	88	33	20	2	1	0
Placebo plus FLOT	474	429	392	360	329	302	278	264	249	202	160	89	65	26	21	2	1	0

	No. of Participants with Event/ Total No. of Participants (%)	Median Event-free Survival (95% CI)
		mo
Durvalumab plus FLOT	167/474 (35.2)	NR (40.74–NR)
Placebo plus FLOT	218/474 (46.0)	32.8 (27.86–NR)

Stratified hazard ratio for event or death, 0.71 (95% CI, 0.58–0.86)
P<0.001 by stratified log-rank test

Janjigian, NEJM 2025

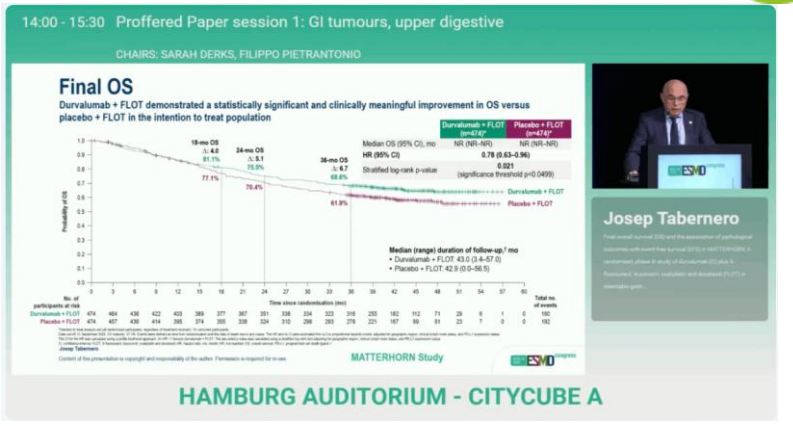
ESMO 2025 : OS



Tabernero, ESMO 2025

ESMO 2025 : OS

- Bénéfice quelque soit :
  - Statut PDL1 (TAP)
  - La localisation (JOG ou Estomac)
  - Le statut N



FLOT + DURVA = STANDARD EN PERI-OP DES CANCERS DE L'ESTOMAC ET DE LA JOG STADES II-IV CHEZ LES PATIENTS OMS 0-1

accès précoce début 2026?

Janjigian, NEJM 2025

DESTINY-gastric04

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Trastuzumab Deruxtecan or Ramucirumab plus Paclitaxel in Gastric Cancer

K. Shitara,[1] E. Van Cutsem,[2,3] M. Gümüş,[4,5] S. Lonardi,[6] C. de la Fouchardière,[7] C. Coutzac,[7] J. Dekervel,[2,3] D. Hochhauser,[8] L. Shen,[9,10] W. Mansoor,[11] B. Liu,[12] L. Fornaro,[13] M.-H. Ryu,[14,15] J. Lee,[16] C. Faustino,[17] J.-P. Metges,[18] J. Tabernero,[19,20] F. Franke,[21] Y.Y. Janjigian,[22] F. Souza,[23] L. Jukofsky,[23] Y. Zhao,[23] T. Kamio,[23] A. Zaanan,[24,25] and F. Pietrantonio,[26] for the DESTINY-Gastric04 Trial Investigators*

2025 ASCO

Shitara, NEJM 2025

DESTINY-gastric04 - Design

Patients

- ADK œso-gastrique prouvé, localement avancé ou M+
- **HER2 + testé avant la L2**
- Progression sous ou après L1 trastuzumab
- ECOG PS 0 ou 1

Stratification

- Statut HER2 (IHC3+ vs IHC2+/ISH+)
- Région (Asie[Chine exclue] vs. Europe W vs Chine/ROW
- Tps jusqu'à progression sous L1 (<6 mois vs ≥6)

R 1:1
N=494

T-DXd 6,4 mg/kg
/ 3 semaines

Ramucirumab 8 mg/kg
J 1, 8, 15 (J1 = J28)
+ Paclitaxel 80 mg/m²
J 1, 8, 15 (J1 = J28)

Objectif primaire :

- SG

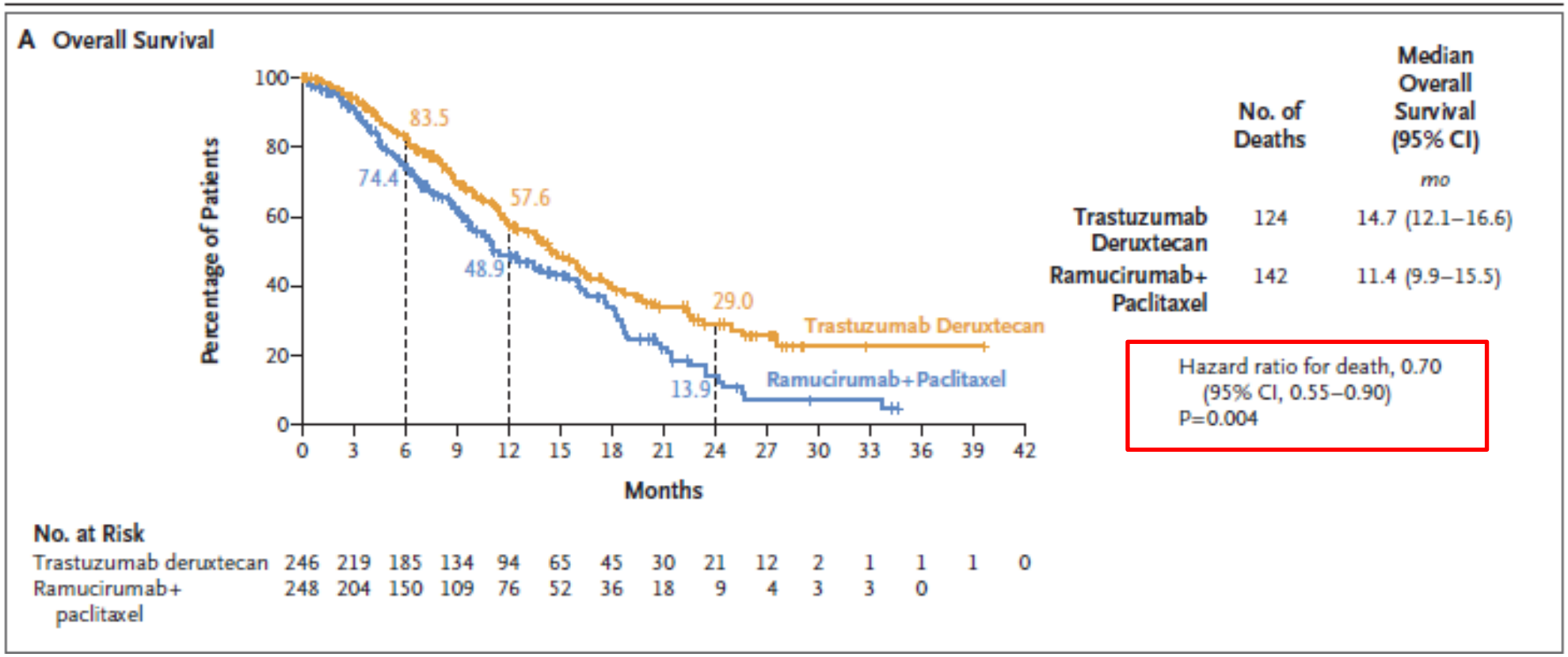
Objectifs secondaires :

- SSP
- Taux de RO, durée de Rép. Et TCM
- Toxicité
- PK

L'actualité en oncologie
30 mai-2 juin 2025
Le Cancer.fr

Shitara, NEJM 2025

DESTINY-gastric04 – SG (CJP)



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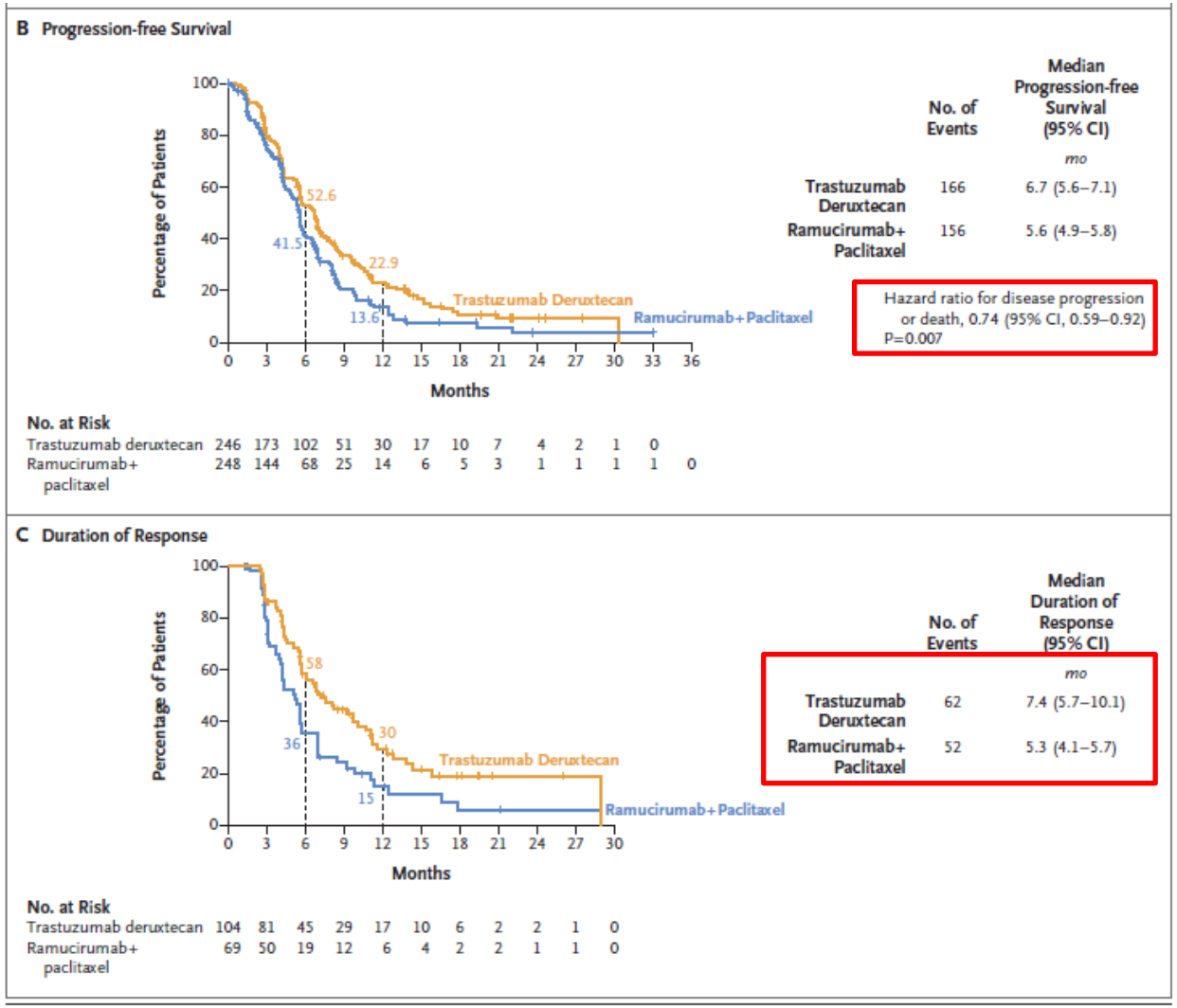
DESTINY-gastric04 – PFS et durée de réponse



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DESTINY-gastric04 – effets secondaires

- Digestif
- Hémato
- Fatigue
- Pneumopathie interstitielle

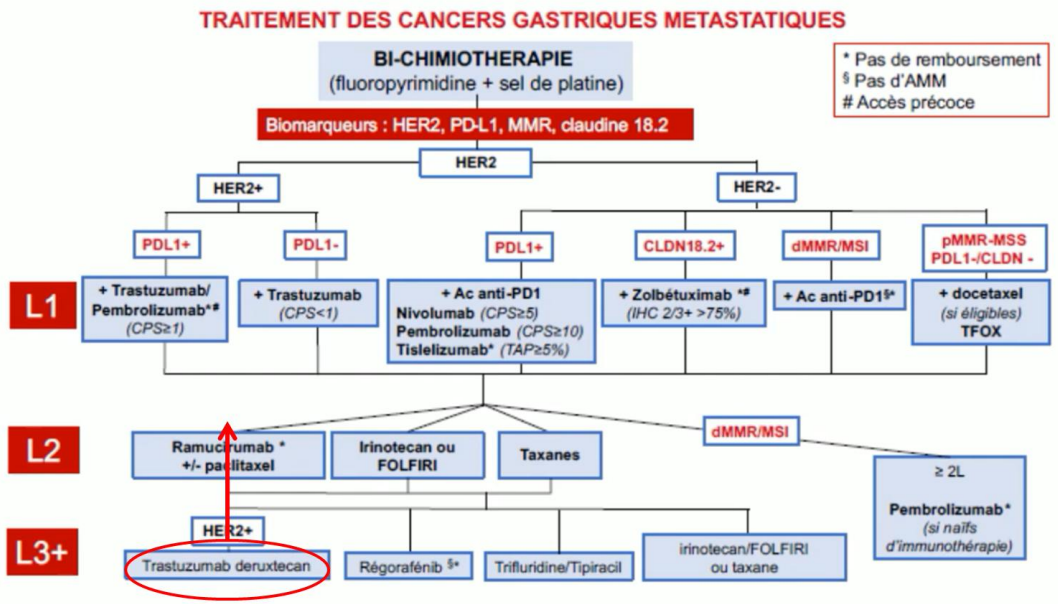
Table 3. Most Common Drug-Related Adverse Events.*

Event	Trastuzumab Deruxtecan (N=244)		Ramucirumab + Paclitaxel (N=233)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
	number of patients with event (percent)			
Any drug-related adverse event	227 (93.0)	122 (50.0)	213 (91.4)	126 (54.1)
Fatigue†	117 (48.0)	17 (7.0)	88 (37.8)	6 (2.6)
Neutropenia‡	117 (48.0)	70 (28.7)	114 (48.9)	83 (35.6)
Nausea	108 (44.3)	12 (4.9)	33 (14.2)	0
Anemia§	76 (31.1)	34 (13.9)	77 (33.0)	32 (13.7)
Decreased appetite	71 (29.1)	5 (2.0)	42 (18.0)	3 (1.3)
Leukopenia¶	65 (26.6)	18 (7.4)	52 (22.3)	29 (12.4)
Thrombocytopenia‖	65 (26.6)	21 (8.6)	32 (13.7)	7 (3.0)
Diarrhea	63 (25.8)	3 (1.2)	47 (20.2)	5 (2.1)
Alopecia	59 (24.2)	0	62 (26.6)	0
Aminotransferase level increased**	53 (21.7)	5 (2.0)	22 (9.4)	1 (0.4)
Vomiting	49 (20.1)	7 (2.9)	16 (6.9)	1 (0.4)
Interstitial lung disease or pneumonitis††	34 (13.9)	1 (0.4)	3 (1.3)	3 (1.3)
Weight decreased	27 (11.1)	3 (1.2)	9 (3.9)	1 (0.4)
Constipation	26 (10.7)	0	12 (5.2)	0
Lymphopenia‡‡	25 (10.2)	5 (2.0)	13 (5.6)	3 (1.3)
Stomatitis§§	12 (4.9)	1 (0.4)	33 (14.2)	1 (0.4)
Neuropathy¶¶	6 (2.5)	0	68 (29.2)	8 (3.4)
Epistaxis	4 (1.6)	0	30 (12.9)	1 (0.4)
Hypertension	1 (0.4)	0	36 (15.5)	19 (8.2)

Shitara, NEJM 2025

DESTINY-gastric04 - Conclusion

- **T-DXd = nouveau standard de 2ème ligne pour les ADK HER+**
- Re-Testing avant la L2
- Place en L1 en cours d'évaluation (DESTINY-gastric05)



Shitara, NEJM 2025

SANO trial

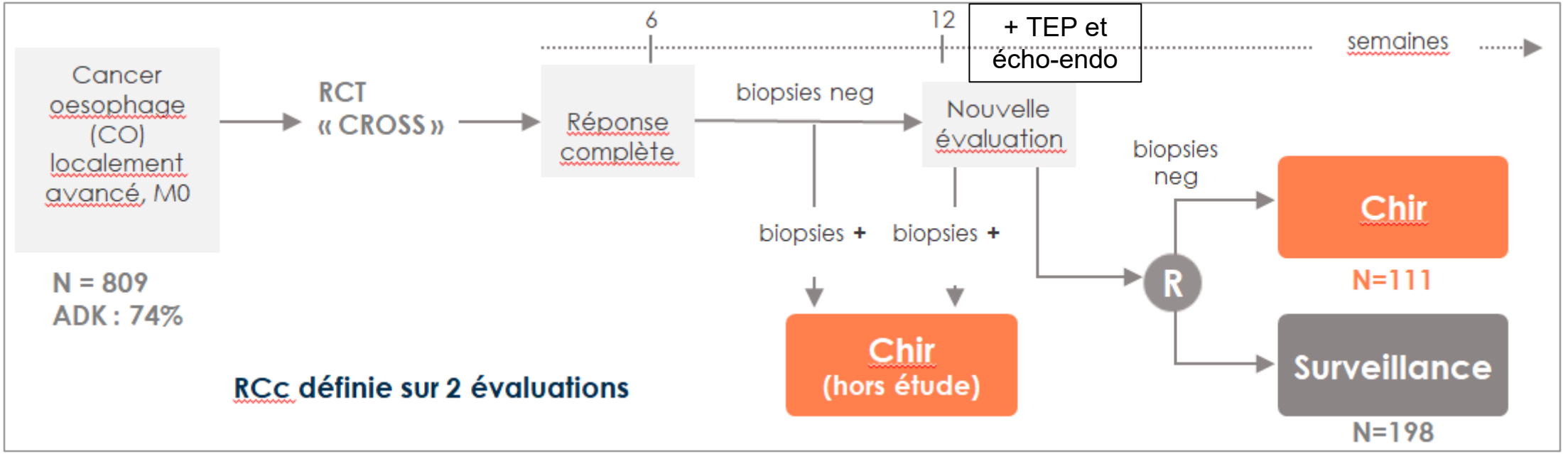
Neoadjuvant chemoradiotherapy followed by active surveillance versus standard surgery for oesophageal cancer (SANO trial): a multicentre, stepped-wedge, cluster-randomised, non-inferiority, phase 3 trial

Berend J van der Wilk*, Ben M Eyck*, Bas P L Wijnhoven, Sjoerd M Lagarde, Camiel Rosman, Bo J Noordman, Maria J Valkema, Tanya M Bisseling, Peter-Paul L O Coene, Marc J van Det, Jan Willem T Dekker, Jolanda M van Dieren, Michail Doukas, Stijn van Esser, W Edward Fiets, Henk H Hartgrink, Joos Heisterkamp, I Lisanne Holster, Bastiaan Klarenbeek, David van Klaveren, Eva Kouw, Ewout A Kouwenhoven, Misha D Luyer, Bianca Mostert, Grard A P Nieuwenhuijzen, Liekele E Oostenbrug, Jean-Pierre Pierie, Johanna W van Sandick, Meindert N Sosef, Manon C W Spaander, Roelf Valkema, Edwin S van der Zaag, Ewout W Steyerberg, J Jan B van Lanschot, SANO Study Group†

MADRID 2023 ESMO congress

Van der Wilk, Lancet Oncol 2025

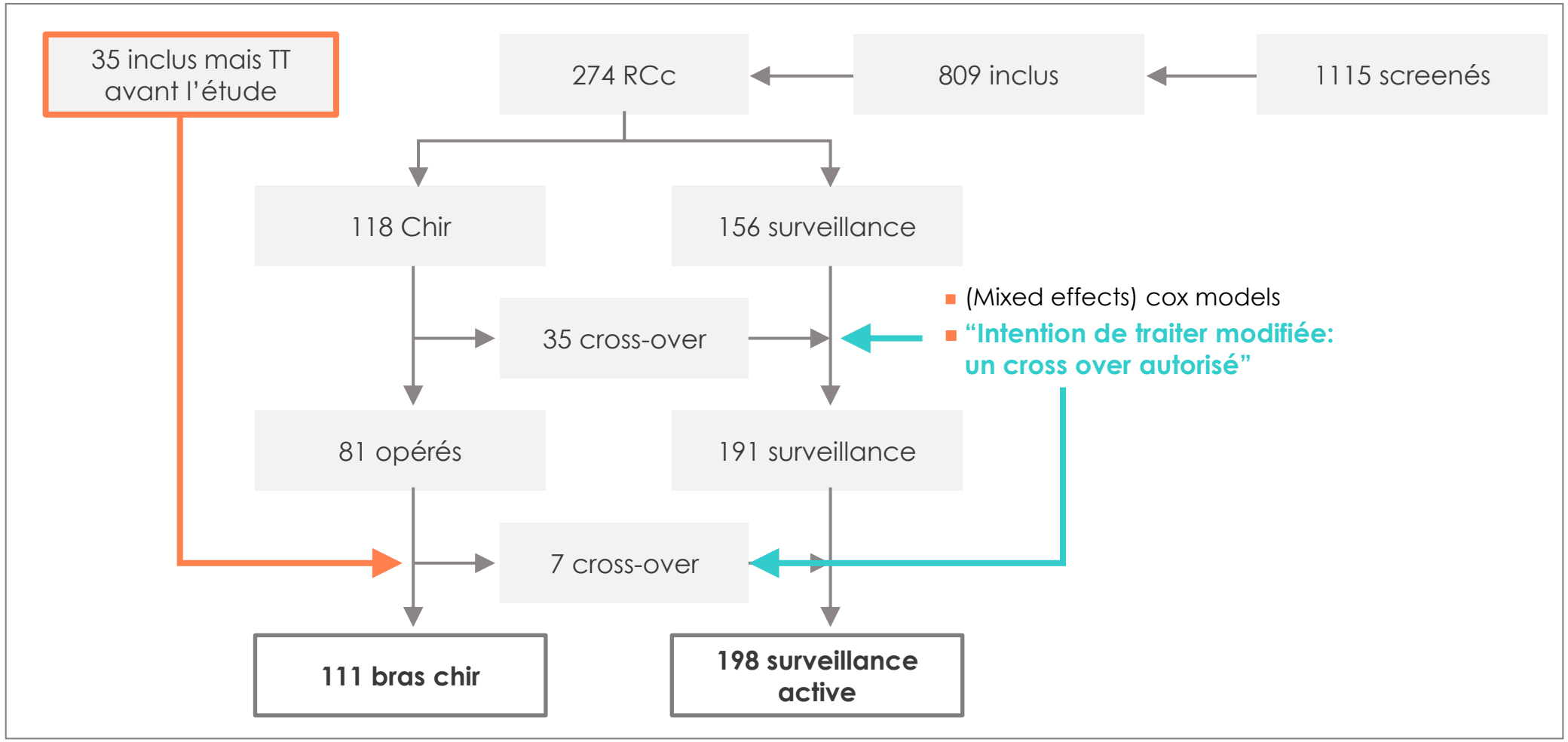
SANO - Design



- Primary endpoint : non-infériorité différence <15% en SG à 2 ans

Van der Wilk, Lancet Oncol 2025

SANO – flow chart



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SANO - Résultats

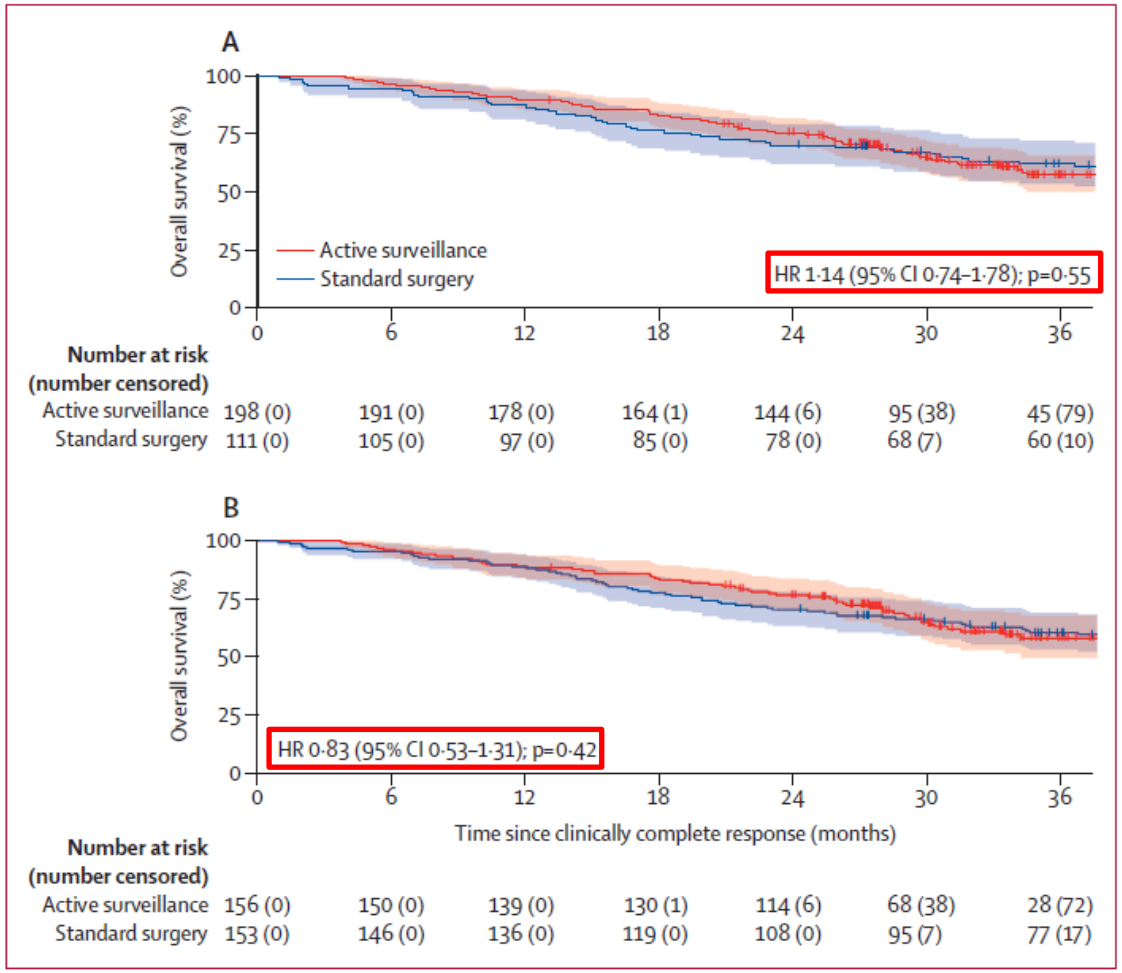

Figure 2: **Kaplan–Meier estimates of overall survival according to modified intention-to-treat analysis (A) and intention-to-treat analysis (B)**

Shaded areas around the curves show 95% CIs. Vertical dashes denote censored patients. CIs were not adjusted for confounders and should not be used for hypothesis testing. HRs are from adjusted analyses. HR=hazard ratio.

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SANO - Résultats

- 34% had CCR

Of whom in active surveillance arm (n=198):

- 33 patients (17%) developed distant metastase (22 within six months)
- 96 (48%) patients developed locoregional regrowth
- 69 patients (35%) had persistent CCR
- 91 patients (46%) had been spared unbeneficial oesophagectomy

SANO – Données chirurgicales

	Active surveillance n= 83/198		Standard surgery n=101
Time to surgery	5.9 months	vs.	0.7 months
R0	81 (98%)	vs.	99 (98%)
Number lymph nodes	23	vs.	25
Operating time (minutes)	304	vs.	338

SANO - Complications

Taux de complications similaires chez les patients opérés

	Active surveillance (n=83)	Standard surgery (n=101)
Any complication	68 (82%)	85 (84%)
Anastomotic leakage	18 (22%)	27 (27%)
Severity of anastomotic leakage		
Subclinical, spontaneous recovery	2 (2%)	3 (3%)
Subclinical, requiring surgery	1 (1%)	0
Clinical, spontaneous recovery	10 (12%)	15 (15%)
Clinical, requiring surgery	5 (6%)	9 (9%)
Pulmonary complications		
Any	39 (47%)	64 (63%)
Pneumonia	20 (24%)	29 (29%)
Respiratory failure requiring reintubation	2 (2%)	5 (5%)
Cardiac complications		
Any	28 (34%)	44 (44%)
Dysrhythmia requiring intervention	11 (13%)	20 (20%)
Vocal cord outcome		
Normal vocal cord	71 (86%)	94 (93%)
Vocal cord dysfunction, unilateral	3 (4%)	3 (3%)
Vocal cord dysfunction, bilateral	2 (2%)	1 (1%)
Unknown vocal cord dysfunction	7 (8%)	3 (3%)
Thromboembolic complications		
Pulmonary embolus	0	2 (2%)
Adverse events from clinical response evaluations		
PET-CT	0	0
Endosonography with fine-needle aspiration	1 (1%)	0
Endoscopy with biopsies	0	0
Chylothorax, requiring TPN	3 (4%)	10 (10%)
Chylothorax, requiring surgery	0	1 (1%)
Multi-organ failure	1 (1%)	1 (1%)
Length of ICU stay, days	2 (1–2)	2 (1–3)
Length of hospital stay, days	10 (8–17)	11 (8–17)
30-day mortality	1 (1%)	3 (3%)
90-day mortality	3 (4%)	5 (5%)

Data are n (%) or median (IQR). Percentages represent the occurrence of complications, as part of the total. TPN=total parenteral nutrition. ICU=intensive care unit.

Table 2: **Postoperative complications and serious adverse events from clinical response evaluations of patients undergoing oesophagectomy**

Van der Wilk, Lancet Oncol 2025

SANO - Conclusion

- **Etude positive**
  - **Pas de différence en SG à 2 ans**
  - **Chirurgie de rattrapage possible sans risque supplémentaire**

- Option de prise en charge?
  - *Standard aux Pays-Bas (avec discussion avec le patient)*
  - Mais approche non recommandée en France pour l'instant
  - Faisabilité d'une surveillance très stricte? *Oui pour le rectum*

- *Essai OESOSTRATE (PRODIGE 32) fermé faute d'inclusion*
- *Essai NEEDS en cours*

Van der Wilk, Lancet Oncol 2025