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MEETING SUMMARY
UPPER GI CANCER HIGHLIGHTS FROM ASCO GI 2023

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DEVELOPED BY GI CONNECT

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THIS PROGRAMME HAS BEEN DEVELOPED BY THE FOLLOWING EXPERTS

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ZOLBETUXIMAB + mFOLFOX6 AS 1L TREATMENT FOR PTS WITH CLDN18.2+ / HER2− LOCALLY ADVANCED UNRESECTABLE OR METASTATIC GASTRIC OR GASTROESOPHAGEAL JUNCTION ADENOCARCINOMA: PRIMARY RESULTS FROM PHASE 3 SPOTLIGHT STUDY

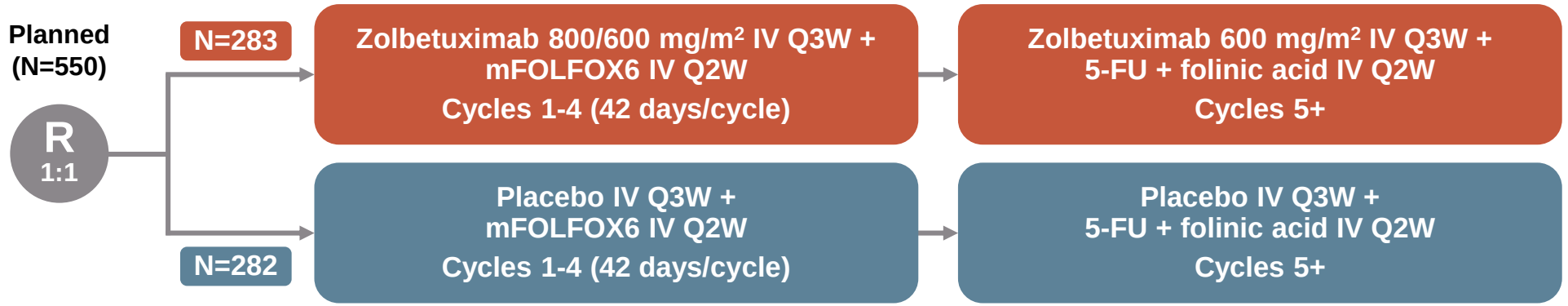
Shitara K, et al. ASCO GI 2023. Abstract #LBA292

1L, first line; CLDN, claudin; FOLFOX, folinic acid, fluorouracil and oxaliplatin; HER2, human epidermal growth factor receptor 2; mFOLFOX(6), modified FOLFOX(6); PT, patient

SPOTLIGHT: BACKGROUND AND STUDY DESIGN

- Patients with unresectable or metastatic G/GEJ adenocarcinoma are often treated with standard of care chemotherapy like mFOLFOX[1-7]
- Targeted therapy prolongs survival in a limited number of patients (e.g. trastuzumab can benefit around 15% of patients with HER2+)[2-9]
- Zolbetuximab is an IgG1 monoclonal antibody that targets CLDN18.2, a tight junction protein that is expressed on the surface of mucosal cells in G/GEJ[10-17]

SPOTLIGHT is a global, randomized, double-blind, placebo controlled phase 3 study[18]



Primary endpoint
- PFS

Key secondary endpoints
- OS
- TTCD in GHS/QoL, PF and OG25-Pain

Secondary endpoints
- ORR
- DoR
- Safety
- PROs

5-FU, fluorouracil; CLDN, claudin; DoR, duration of response; FOLFOX, folinic acid, fluorouracil and oxaliplatin; G/GEJ, gastric or gastroesophageal junction; GHS, global health status; HER2, human epidermal growth factor receptor 2; IV, intravenous; mFOLFOX(6), modified FOLFOX(6); OG25, oesophageal module questionnaire; ORR, objective response rate; OS, overall survival; PF, physical function; PFS, progression-free survival; PRO, patient-reported outcome; Q2/3W, every 2/3 weeks; R, randomisation; TTCD, time to confirmed clinical deterioration

1. Van Cutsem et al. Lancet. 2016;388:2654-64; 2. Lordick F, et al. Ann Oncol. 2022;33:1005-20; 3. Obermannová R, et al. Ann Oncol. 2022;33:992-1004; 4. JGCA. Gastric Cancer 2021;24:1-21; 5. Kelly RJ, et al. New Engl J Med. 2021;384:1191-1203; 6. NHCPRC. Chin J Cancer Res. 2022;34:207-37; 7. Bang Y-J, et al. Lancet 2010;376:687-97; 8. Janjigian YY, et al. Lancet 2021;398:27-40; 9. Shitara K, et al. Nature. 2022;603:942-8; 10. Nimi T, et al. Mol Cell Biol. 201;21:7380-90; 11. Sahin U, et al. Clin Cancer Res. 2008;14:7624-34; 12. Moran D, et al. Ann Oncol. 2018;29:viii13-viii57; 13. Sahin U, et al. Eur J Cancer. 2018;100:17-26; 14. Rohde C, et al. Jpn J Clin Oncol. 2019;49:870-76; 15. Türeci Ö, et al. Ann Oncol. 2019;30:1487-95. 16. Pellino A, et al. J Pers Med. 2021;11:1095; 17. Sahin U et al. Ann Oncol. 2021;32:609-19; 18. https://www.clinicaltrials.gov/ct2/show/NCT03504397 (last accessed: January 25, 2023)

SPOTLIGHT: RESULTS

- Primary Endpoint: PFS was significantly longer in patients treated with zolbetuximab + mFOLFOX vs placebo + mFOLFOX
- Secondary Endpoint: OS was significantly longer in patients treated with zolbetuximab + mFOLFOX vs placebo + mFOLFOX
- Incidence of TEAEs were similar in both treatment arms
  - GI toxicity was the most common

Primary endpoint: PFS

	mFOLFOX6	mFOLFOX6
No. events/ no. patients	146/283	167/282
Median PFS, months (95% CI)	10.61 (8.90-12.48)	8.67 (8.21-10.28)
HR (95% CI) p value	0.751 (0.589-0.942) 0.0066	

Key secondary endpoint: OS

	Zolbetuximab + mFOLFOX6	Placebo + mFOLFOX6
No. events/ no. patients	149/283	177/282
Median OS, months (95% CI)	18.23 (16.43-22.90)	15.54 (13.47-16.53)
HR (95% CI) p value	0.750 (0.601-0.936) 0.0053	

CI, confidence interval; FOLFOX, folinic acid, fluorouracil and oxaliplatin; GI, gastrointestinal; HR, hazard ratio; mFOLFOX(6), modified FOLFOX(6); OS, overall survival; PFS, progression-free survival; TEAE, treatment-emergent adverse event

SPOTLIGHT: RESULTS

ADVERSE EVENTS IN ALL TREATED PATIENTS

Event, n (%)	Zolbetuximab + mFOLFOX6 (N=279)		Placebo + mFOLFOX6 (N=278)	
	All Grade	Grade ≥3	All Grade	Grade ≥3
All TEAEs	278 (99.6)	242 (86.7)	277 (99.6)	216 (77.7)
Serious TEAEs	125 (44.8)	–	121 (43.5)	–
TRAEs leading to discontinuation of any study drug	106 (38.0)	–	82 (29.5)	–
TRAEs leading to discontinuation of zolbetuximab or placebo	38 (13.6)	–	6 (2.2)	–
TRAEs leading to death	5 (1.8)		4 (1.4)	

FOLFOX, folinic acid, fluorouracil and oxaliplatin; mFOLFOX(6), modified FOLFOX(6); TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event

SPOTLIGHT: SUMMARY

- Treatment with zolbetuximab + mFOLFOX showed a statistically and clinically significant improvement for PFS and OS
  - These benefits were also seen across most subgroups of patients
- Zolbetuximab + mFOLFOX demonstrated a tolerable and manageable safety profile
- Zolbetuximab + mFOLFOX is potentially a new standard of care treatment for unresectable or metastatic G/GEJ patients with CLDN18.2 +ve / HER2−ve biomarker profile

Clinical Takeaways:

- **SPOTLIGHT results indicate that patients expressing Claudin 18.2 could potentially benefit from this agent**
- **Incorporation of this agent still remains a question and oncologists need to discuss patient selection methods**
- **Tissue claudin 18.2 expression needs to be incorporated into lab testing**

CLDN, claudin; FOLFOX, folinic acid, fluorouracil and oxaliplatin; G/GEJ, gastric or gastroesophageal junction; HER2, human epidermal growth factor receptor 2; mFOLFOX, modified FOLFOX; OS, overall survival; PFS, progression-free survival

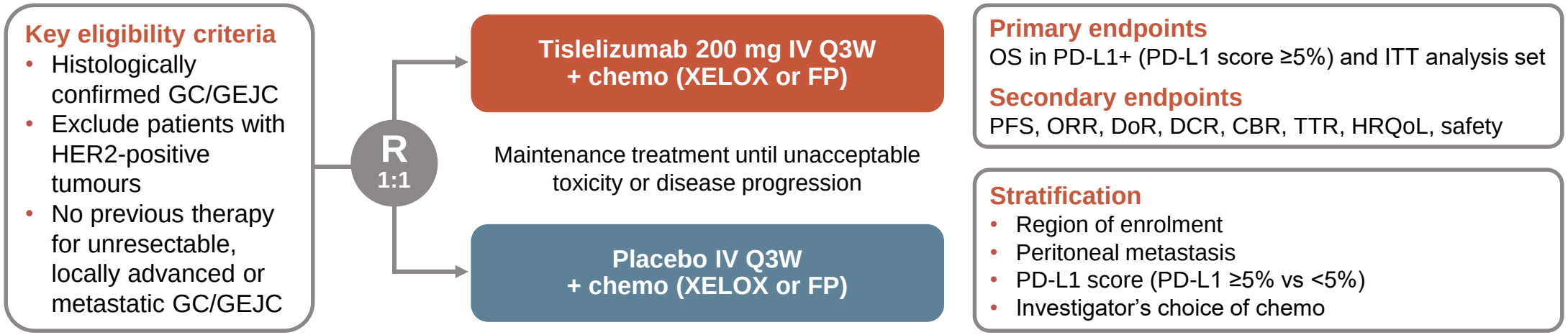
RATIONALE 305: PHASE 3 STUDY OF TISLELIZUMAB PLUS CHEMOTHERAPY VS PLACEBO PLUS CHEMOTHERAPY AS 1L TREATMENT OF ADVANCED GASTRIC OR GASTROESOPHAGEAL JUNCTION ADENOCARCINOMA

Moehler M, et al. ASCO GI. Abstract #286

1L, first line

RATIONALE 305: BACKGROUND AND STUDY DESIGN

- G/GEJ cancer has a poor prognosis[1]. The addition of the anti-(PD-1) treatment, nivolumab, to standard of care has already been approved for first line treatment of G/GEJ cancer[2-4]
- Tislelizumab is an anti-PD-1 monoclonal antibody engineered to minimize binding to FcγR on macrophages[5]
- The **Rationale 305** study is a randomised, double-blind, global phase 3 study[6]



CBR, clinical benefit rate; DCR, disease control rate; DoR, duration of response; FcγR, Fc gamma receptor; FP, 5-FU/cisplatin; G/GEJ, gastric or gastroesophageal junction; HER2, human epidermal growth factor receptor 2; HRQoL, health-related quality of life; ITT, intent to treat; IV, intravenous; ORR, objective response rate; OS, overall survival; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1; PFS, progression-free survival; Q3W, every 3 weeks; TTR, time to recurrence; XELOX, oxaliplatin and oral capecitabine

1. Patel TH and Cecchini M. Curr Treat Options Oncol. 2020;21:70; 2. US Food and Drug Administration. Available at: http://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-nivolumab-combination-chemotherapy-metastatic-gastric-cancer-and-esophageal (last accessed: January 25, 2023); 3. PPF. Available at: https://www.ppf.eu/en/insights/biotech-market/september-2021-review-of-news-from-the-most-innovative-therapeutic-areas-and-the/opdivo-approved-as-first-immunotherapy-for-first-line-advanced-gastric-cancer-in (last accessed: January 25, 2023); 4. Bristol Myers Squibb press release. Available at: https://news.bms.com/news/corporate-financial/2021/Bristol-Myers-Squibb-Receives-European-Commission-Approval-for-Opdivo-nivolumab--Chemotherapy-for-Patients-with-HER2-Negative-Advanced-or-Metastatic-Gastric-Gastroesophageal-Junction-or-Esophageal-Adenocarcinoma-/default.aspx (last accessed: January 25, 2023); 5. Zhang T, et al. Cancer Immunol Immunother. 2018;67:1079-90; 6. https://clinicaltrials.gov/ct2/show/NCT03777657 (last accessed: January 25, 2023)

RATIONALE 305: RESULTS

- Overall Survival (OS): TIS plus chemo demonstrated statistically significant improvement in OS vs placebo plus chemo
- Progression free survival (PFS): TIS plus chemo demonstrated improvement in PFS vs placebo plus chemo
- Numerically higher ORR and more durable response for TIS plus chemo vs placebo + chemo

Overall survival

	TIS + Chemo	Placebo + Chemo
Events, n (%)	130 (47.4)	161 (59.2)
Median OS, months (95% CI)	**17.2 (13.9, 21.3)**	**12.6 (12.0, 14.4)**
HR (95% CI)	0.74 (0.59, 0.94)	
p value	0.0056	

Progression-free survival

	TIS + Chemo	Placebo + Chemo
Events, n (%)	169 (61.7)	206 (75.7)
Median PFS, months (95% CI)	**7.2 (5.8, 8.4)**	**5.9 (5.6, 7.0)**
HR (95% CI)	0.67 (0.55, 0.83)	

CI, confidence interval; HR, hazard ratio; ORR, objective response rate; TIS, tislelizumab

RATIONALE 305: SUMMARY

- TIS plus chemo had a manageable safety profile in patients with unresectable, locally advanced or metastatic G/GEJ cancer
- TIS plus chemo demonstrated statistically significant and clinically meaningful improvement in OS versus placebo plus chemo in patients with PD-L1-positive GC/GEJ cancer.
  - Median OS: 17.2 vs 12.6 months; HR 0.74 (95% CI 0.59, 0.94); p=0.0056
- RATIONALE-305 results provide tislelizumab plus chemotherapy as a new 1L treatment option for patients with PD-L1-positive unresectable, locally advanced or metastatic GC/GEJ cancer
- Double blind treatment within the study is still ongoing and results of the final analysis for OS will be presented later this year

Clinical takeaway:

- **Towards the goal of developing an immunotherapy in PD-L1+ve patients, tislelizumab - like nivolumab - shows promising results**

1L, first line; CI, confidence interval; G/GEJ, gastric or gastroesophageal junction; HR, hazard ratio; ITT, intent to treat; OS, overall survival; PD-L1, programmed death ligand 1; TIS, tislelizumab

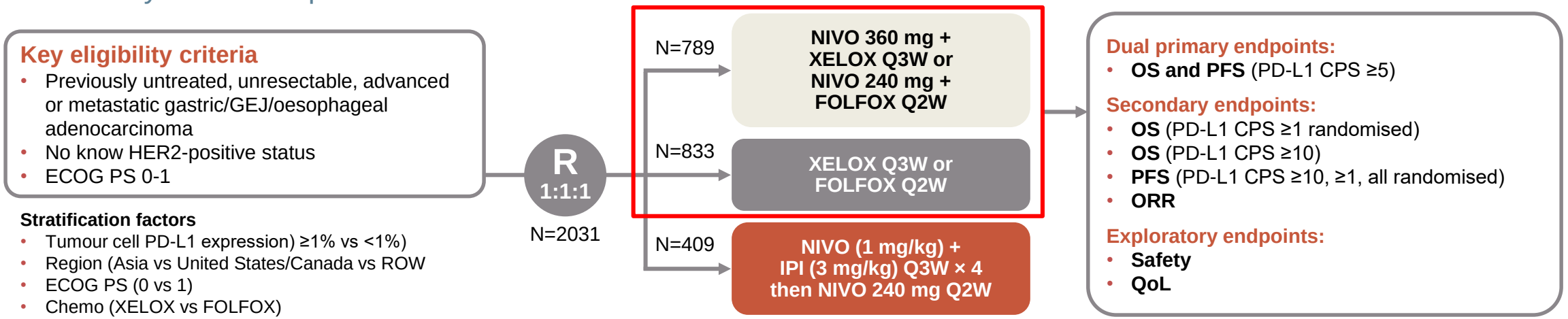
NIVO PLUS CHEMO VS CHEMO AS 1L TREATMENT FOR ADVANCED GASTRIC CANCER/GASTROESOPHAGEAL JUNCTION CANCER/ESOPHAGEAL ADENOCARCINOMA: 3-YEAR FOLLOW-UP FROM CHECKMATE 649

Janjigian Y, et al. ASCO GI 2023. Abstract #291

1L, first line; chemo, chemotherapy; NIVO, nivolumab

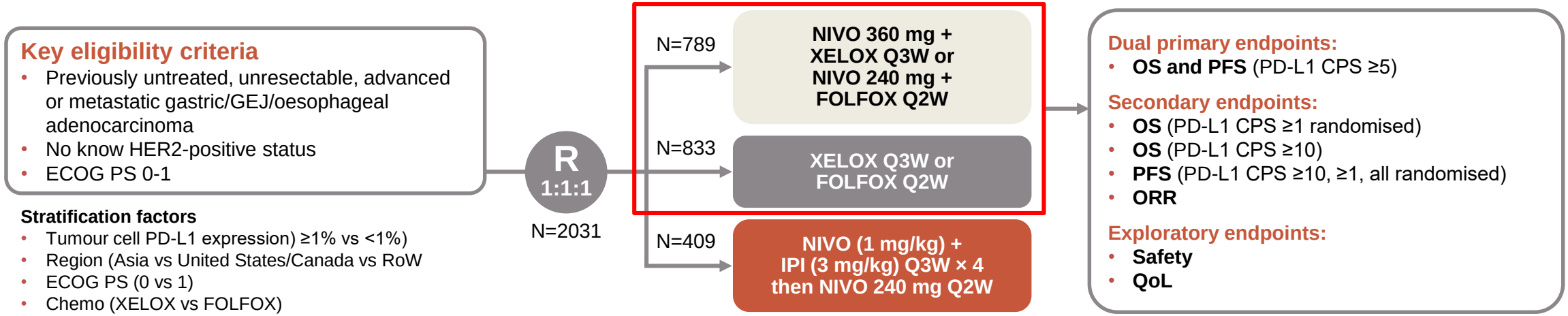
CHECKMATE 649: BACKGROUND AND STUDY DESIGN

- Randomised open-label, global phase 3 study
- Patients enrolled from 175 hospital and cancer centres in 29 countries
- At data cutoff (May 31st 2022) minimum follow up was 36.2 months
- NIVO + chemo demonstrated superior OS and clinically meaningful PFS benefit vs chemo and an acceptable safety profile after 1 year of follow-up in previously untreated patients with advanced GC/GEJC/EAC in CheckMate 649
- The combination is currently approved in more than 50 countries
- The 3-year follow-up results from the NIVO+ chemo vs chemo arms of CheckMate 649



CHECKMATE 649: BACKGROUND AND STUDY DESIGN

- NIVO + chemo demonstrated superior OS and clinically meaningful PFS benefit vs chemo and an acceptable safety profile after 1 year of follow-up in previously untreated patients with advanced GC/GEJC/EAC in CheckMate 649[1]
- The combination is currently approved in more than 50 countries[2-5]
- 3-year follow-up results from the NIVO + chemo vs chemo arms of CheckMate 649 are reported[6]



- Randomised, open-label, global phase 3 study
- Pts enrolled from 175 hospitals / cancer centres, 29 countries
- At data-cut-off (May 31, 2022), minimum FU of 36.2 months

CPS, combined positive score; EAC, oesophageal cancer; ECOG PS, Eastern Cooperative Group Oncology Group performance status; FOLFOX, folinic acid, fluorouracil and oxaliplatin; FU, follow-up; GC, gastric cancer; GEJC, gastroesophageal junction cancer; HER2, human epidermal growth factor receptor 2; IPI, ipilimumab; NIVO, nivolumab; ORR, objective response rate; OS, overall survival; Q2/3W, every 2/3 weeks; PD-L1, programmed cell death ligand 1; PFS, progression-free survival; pt, patient; QoL, quality of life; R, randomisation; RoW, rest of world; XELOX, oxaliplatin and oral capecitabine

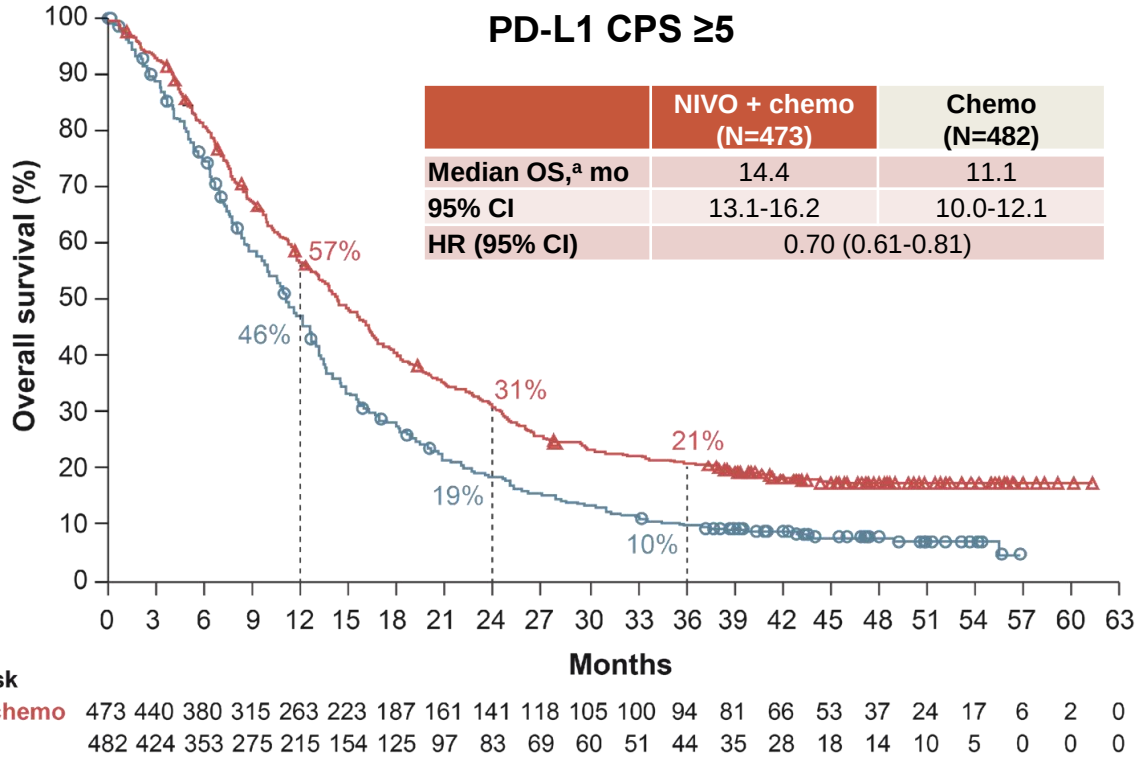
1. Janjigian YY, et al. Lancet. 2021;398:27:40; 2. OPDIVO® (nivolumab) [package insert]. Princeton, NJ: Bristol Myers Squibb, May 2022; 3. OPDIVO® (nivolumab) [package insert]. China: Bristol Myers Squibb, June 2022; 4. OPDIVO® (nivolumab) [SmPC]. Dublin, Ireland: Bristol Myers Squibb, January 2022; 5. OPDIVO® (nivolumab) [package insert]. Japan: Bristol Myers Squibb, July 2022; 6. https://clinicaltrials.gov/ct2/show/NCT02872116 (last accessed: January 25, 2023)

CHECKMATE 649: RESULTS
Overall survival

- After 3 years of follow-up NIVO + chemo continues to show clinically meaningful impact
  - Higher OS / PFS vs chemo at 36 months

OVERALL SURVIVAL: 36-MONTH FOLLOW-UP

PD-L1 CPS ≥5

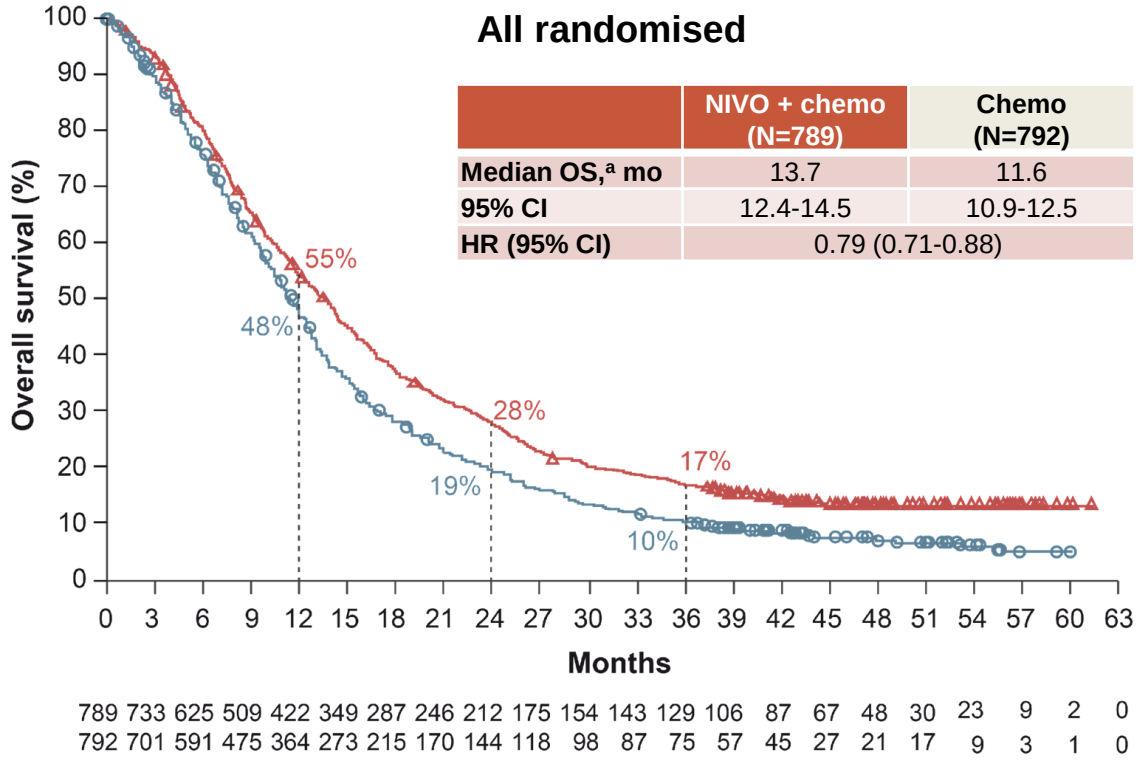


	NIVO + chemo (N=473)	Chemo (N=482)
Median OS,[a] mo	14.4	11.1
95% CI	13.1-16.2	10.0-12.1
HR (95% CI)	0.70 (0.61-0.81)	

No. at risk

NIVO + chemo	473	440	380	315	263	223	187	161	141	118	105	100	94	81	66	53	37	24	17	6	2	0
Chemo	482	424	353	275	215	154	125	97	83	69	60	51	44	35	28	18	14	10	5	0	0	0

All randomised



	NIVO + chemo (N=789)	Chemo (N=792)
Median OS,[a] mo	13.7	11.6
95% CI	12.4-14.5	10.9-12.5
HR (95% CI)	0.79 (0.71-0.88)	

NIVO + chemo	789	733	625	509	422	349	287	246	212	175	154	143	129	106	87	67	48	30	23	9	2	0
Chemo	792	701	591	475	364	273	215	170	144	118	98	87	75	57	45	27	21	17	9	3	1	0

Minimum follow-up, 36.2 months

CI, confidence interval; CPS, combined positive score; HR, hazard ratio; mo, months; NIVO, nivolumab; OS, overall survival; PD-L1, programmed cell death ligand 1; PFS, progression-free survival

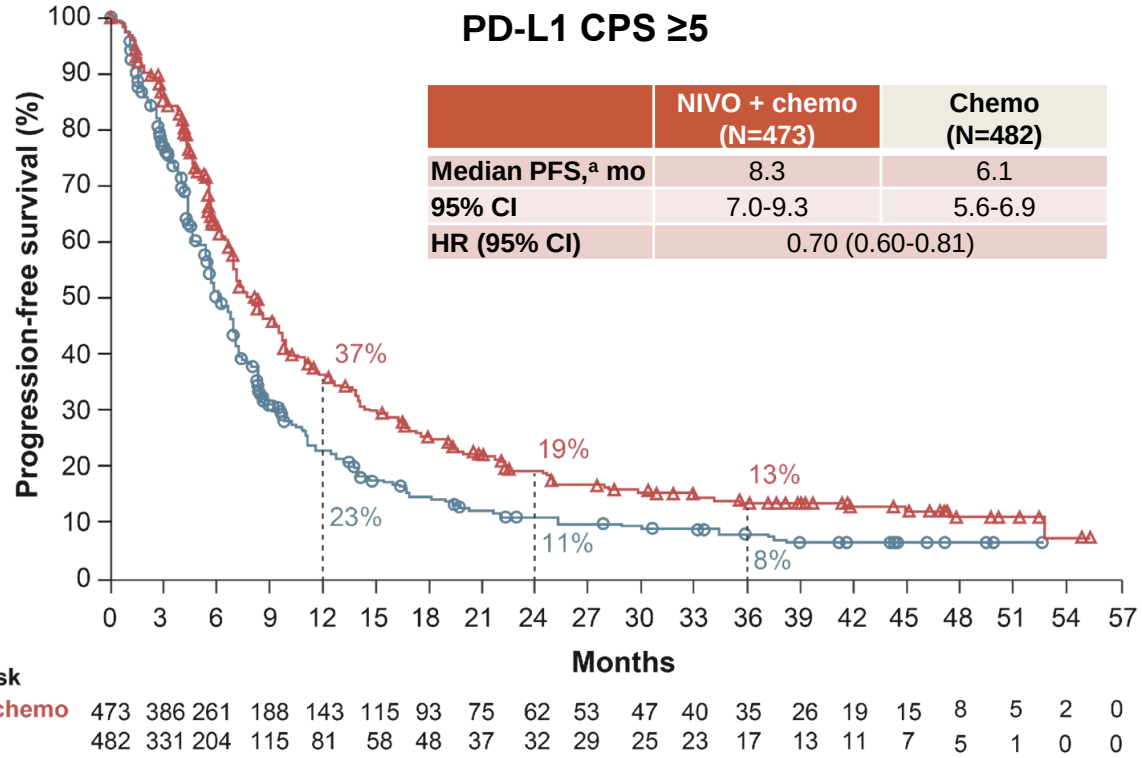
CHECKMATE 649: RESULTS
Progression-free survival

- After 3 years of follow-up NIVO + chemo continues to show clinically meaningful impact
  - Higher OS / PFS vs chemo at 36 months

PROGRESSION-FREE SURVIVAL: 36-MONTH FOLLOW-UP

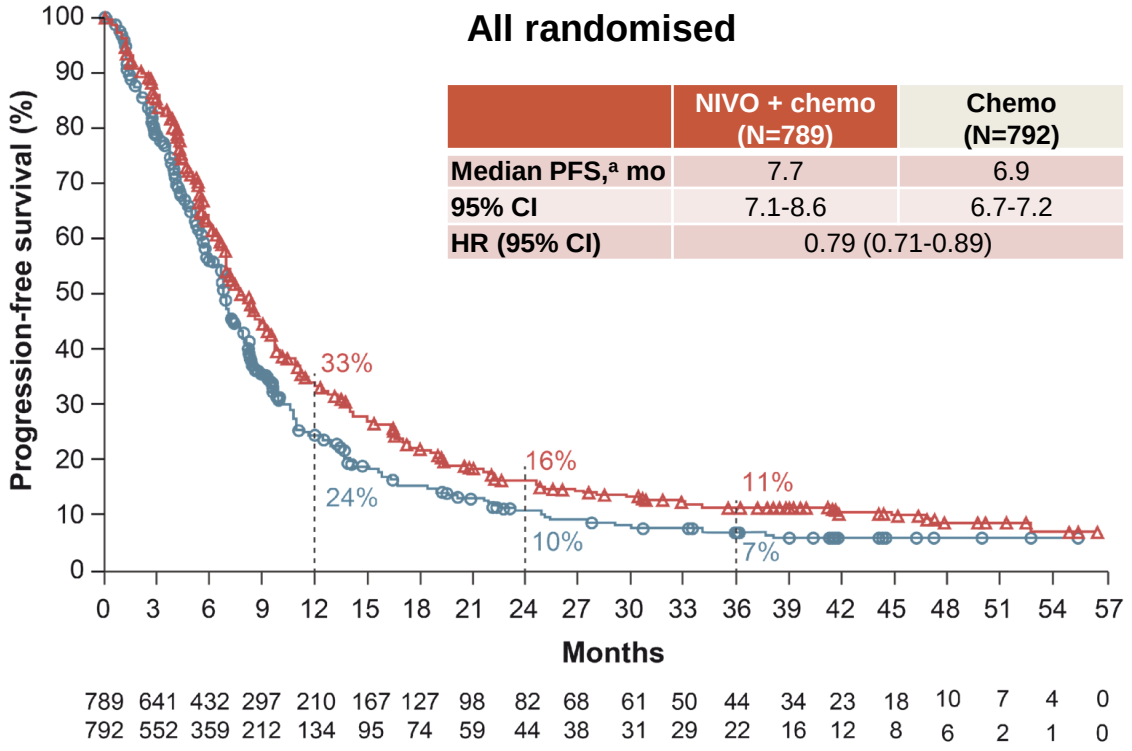
PD-L1 CPS ≥5

	NIVO + chemo (N=473)	Chemo (N=482)
Median PFS,[a] mo	8.3	6.1
95% CI	7.0-9.3	5.6-6.9
HR (95% CI)	0.70 (0.60-0.81)	



All randomised

	NIVO + chemo (N=789)	Chemo (N=792)
Median PFS,[a] mo	7.7	6.9
95% CI	7.1-8.6	6.7-7.2
HR (95% CI)	0.79 (0.71-0.89)	



Minimum follow-up, 36.2 months

CI, confidence interval; CPS, combined positive score; HR, hazard ratio; mo, months; NIVO, nivolumab; OS, overall survival; PD-L1, programmed cell death ligand 1; PFS, progression-free survival

CHECKMATE 649: SUMMARY

- NIVO + chemo has demonstrated higher ORR across all evaluated PD-L1 CPS subgroups
- No new safety signals were shown with longer follow-up

Clinical takeaway:

- **Data further supports the use of NIVO + chemo in first-line setting for treatment of patients with advanced GC/GEJC/EAC**

CPS, combined positive score; GC, gastric cancer; GEJC, gastroesophageal junction cancer; NIVO, nivolumab; ORR, objective response rate; PD-L1, programmed cell death ligand 1

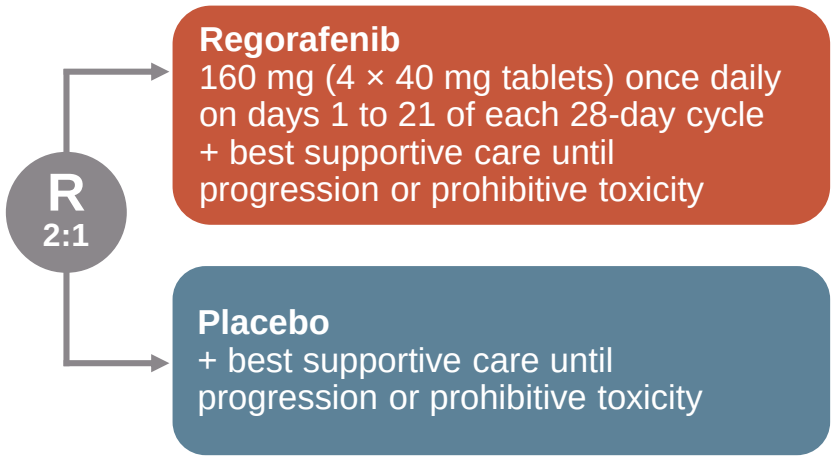
INTEGRATE IIA: A RANDOMISED, DOUBLE-BLIND, PHASE 3 STUDY OF REGORAFENIB VERSUS PLACEBO IN REFRACTORY ADVANCED GASTRO-OESOPHAGEAL CANCER – A STUDY LED BY THE AUSTRALASIAN GASTROINTESTINAL TRIALS GROUP (AGITG)

Pavlakis N, et al. ASCO GI 2023. Abstract #LBA294

INTEGRATE IIA: BACKGROUND AND STUDY DESIGN

- Refractory advanced gastric and oesophago-gastric junction cancer has limited treatment options[1]
- Regorafenib is a multi-targeted tyrosine kinase inhibitor (TKI)[2]
  - Prolonged survival vs placebo in all regions and subgroups in the **INTEGRATE** phase 2 trial[2]

INTEGRATE IIa: *an international, multicentre, randomised phase 3 study*[3]



Endpoints

- **Primary:** OS
- **Secondary:** PFS, Objective Tumour Response Rate, QoL, EORTC QLQ-C30 and STO22), Safety (NCI-CTCAE v 4.03)
- **Tertiary:** Pharmacokinetics, Biomarkers

Stratification

- Tumour location (gastro-oesophageal junction vs stomach)
- Geographic region (Asia vs Rest of World)
- Prior VEGF inhibitors (Yes vs No)

- **Primary objective** (INTEGRATE IIa): overall survival in ITT patient populations

EORTC, European Organisation for Research and Treatment of Cancer; G/GEJ, gastric or gastroesophageal junction; ITT, intent to treat; NCI-CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Event; OS, overall survival; PFS, progression-free survival; QoL, quality of life; QLQ-C30, EORTC core quality of life questionnaire; QLQ-STO22, EORTC-QLQ-stomach module; R, randomisation; VEGF, vascular endothelial growth factor

1. Smyth EC, et al. Lancet. 2020;396:635-48; 2. Pavlakis N, et al. J Clin Oncol. 2016;34:2728-35; 3. https://clinicaltrials.gov/ct2/show/NCT02773524 (last accessed: January 25, 2023)

INTEGRATE IIA: RESULTS

- Regorafenib improved OS and PFS
- Regorafenib delayed deterioration in global QoL
- Regorafenib toxicity profile was similar to that seen previously

OS, overall survival; PFS, progression-free survival; QoL, quality of life

INTEGRATE IIA: RESULTS

- **Regorafenib improved both overall survival and progression free survival**

INTEGRATE IIa: *regorafenib vs PBO*

	Hazard ratio	95% CI	p value
Overall survival	0.68	0.52-0.90	0.006
Progression-free survival	0.53	0.40–0.70	<0.0001

- Regorafenib delayed deterioration in global QoL vs PBO (p=0.0043)
- Regorafenib toxicity profile was similar to that seen previously

CI, confidence interval; PBO, placebo; QoL, quality of life

INTEGRATE IIA: SUMMARY

- Regorafenib significantly improved survival vs placebo in patients with refractory advanced gastric and esophago-gastric junction cancer
- This benefit is consistent across all pre-planned subgroups
- This is a new treatment option for patients in this setting
- INTEGRATE IIb is another ongoing phase 3 trial in pre-treated patients with refractory advanced gastric and esophago-gastric junction cancer
  - Patients treated with regorafenib + nivolumab vs standard therapy

Clinical takeaway:

- **INTEGRATE IIa study had statistically significant results, although the absolute numbers were not as clinically relevant. Results of INTEGRATE IIb are eagerly awaited to further understand the utility of this agent in this disease setting**

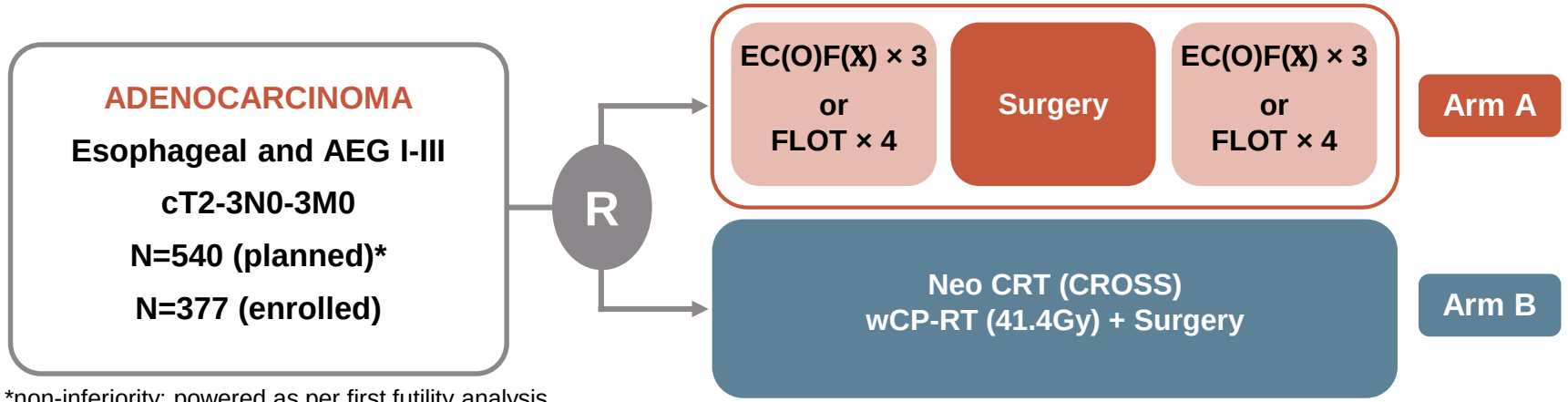
NEO-AEGIS (NEOADJUVANT TRIAL IN ADENOCARCINOMA OF THE ESOPHAGUS AND ESOPHAGO-GASTRIC JUNCTION INTERNATIONAL STUDY): FINAL PRIMARY OUTCOME ANALYSIS

John V. R, et al. ASCO GI 2023. Abstract #295

NEO-AEGIS: BACKGROUND AND STUDY DESIGN

- Pathology: Adenocarcinoma, AEG I-III, <8 cm primary tumour length, cT2-3, N (any), AJCC 7th edition[1,2]
- Operative complications: strictly defined (i) as per the Esophageal Complications Consensus Group (ECCG), and (ii) Clavien-Dindo severity score[1,2]

Neo-AEGIS (Arm A: 2013-18 MAGIC; 2018-20; FLOT or MAGIC)[3]



*non-inferiority: powered as per first futility analysis (n=71 deaths)

Primary endpoints:
- Overall survival

Secondary endpoints:
- Disease free survival
- Time to treatment failure
- Toxicity
- Tumour Regression Grade (TRG)
- R0 resection
- Postoperative complications (ECCG defined, Clavien-Dindo)
- Quality of life

AEG, adenocarcinoma of the esophagogastric junction; AJCC, American Joint Committee on Cancer; CROSS, Chemoradiotherapy for Oesophageal Cancer Followed by Surgery Study; CRT, chemoradiotherapy; cT, clinical T stage; FLOT, docetaxel, 5-FU, leucovorin, oxaliplatin; MAGIC, epirubicin, cisplatin (oxaliplatin), 5-FU (capecitabine); M, evaluation of distant metastasis; N, evaluation of regional lymph nodes

1. Low D, et al. Ann Surg. 2015;262:286-94; 2. Dindo D, et al. Ann Surg. 2004;240:205-113; 3. https://clinicaltrials.gov/ct2/show/NCT01726452 (last accessed: January 25, 2023)

NEO-AEGIS: RESULTS AND SUMMARY

- Peri-operative chemotherapy does not seem inferior to neoadjuvant chemoradiotherapy CROSS-regimen
- The 3-year survival is 55% for peri-operative chemotherapy and 57% for CROSS regimen
- However, markers of response including pathologic complete response, major pathologic response, R0 rate and nodal-down staging, were significantly better in CROSS arm
- There was no significant difference between regimens in severity of complications
- Data will support better clinical decision-making

Clinical takeaway:

- **Peri-operative chemotherapy and neoadjuvant chemoradiotherapy CROSS regimen have similar overall survival results. The data should make it easier for clinicians to decide between CROSS and peri-operative chemotherapy, particularly as CROSS is associated with lower toxicity**

CROSS, Chemoradiotherapy for Oesophageal Cancer Followed by Surgery Study

INFINITY: A MULTICENTRE, SINGLE-ARM, MULTI-COHORT, PHASE 2 TRIAL OF TREMELIMUMAB AND DURVALUMAB AS NEOADJUVANT TREATMENT OF PATIENTS WITH MSI HIGH RESECTABLE GASTRIC OR GASTROESOPHAGEAL JUNCTION ADENOCARCINOMA

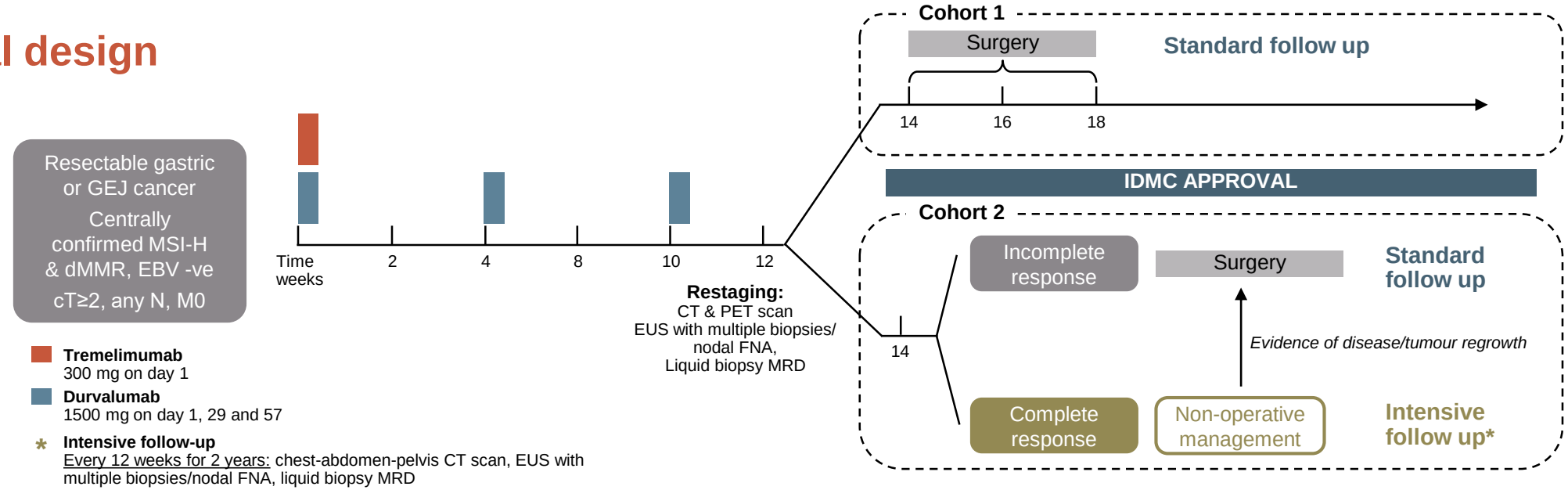
Filippo P, et al. ASCO GI 2023. Abstract #358

MSI, microsatellite instability

INFINITY: BACKGROUND AND STUDY DESIGN

- In resectable G/GEJ cancer, dMMR/MSI-H status is associated with better survival and a potential lack of benefit from chemotherapy[1]
- dMMR/MSI-H status is one of the strong predictors of the efficacy of immunotherapy[2]
- INFINITY is a multicentre, single arm and phase 2 clinical study[3]

Trial design



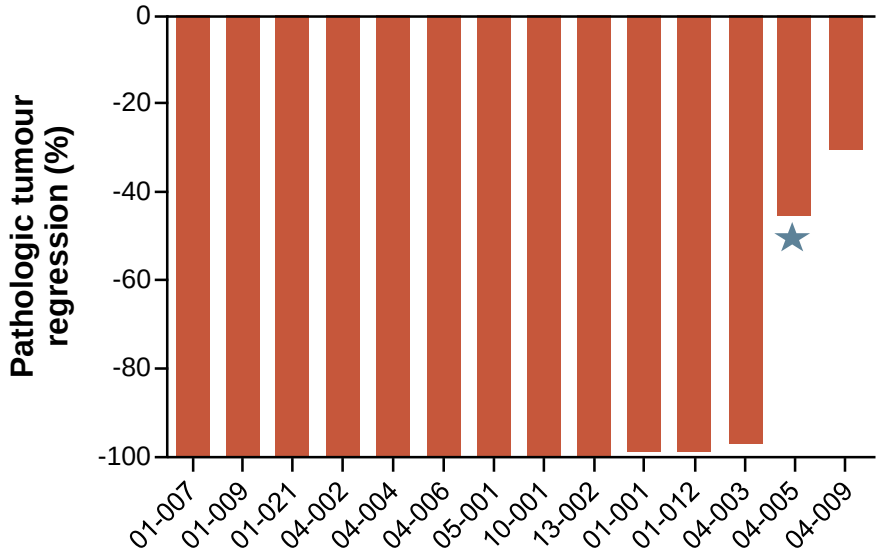
cT, clinical T stage; CT, computed tomography; dMMR, DNA mismatch repair deficiency; EBV, Epstein-Barr virus; EUS, endoscopic ultrasound; FNA, fine-needle aspiration; G/GEJ, gastric or gastroesophageal junction; IDMC, independent data monitoring committee; M, evaluation of distant metastasis; MRD, minimal residual disease; MSI-H, microsatellite instability-high; N, evaluation of regional lymph nodes; PET, positron emission tomography

1. Pietrantonio F, et al. J Clin Oncol. 2019;37:3392-400; 2. Leone AG, et al. ESMO Open. 2022;7:100380; 3. https://clinicaltrials.gov/ct2/show/NCT04817826 (last accessed: January 25, 2023)

INFINITY: RESULTS

- Primary endpoint: pathological complete response (ypT0N0) and negative ctDNA status after neoadjuvant immunotherapy

Primary endpoint



TRG Becker	N=15	%
1a	9	60%
1b	3	20%
3	2	13%

1 patient did not undergo surgery for PD

Among evaluable patients, rate of pCR was 60% and rate of major to complete pathological response (<10% viable cells) was 80%

★ Heterogeneous pMMR/dMMR status at surgery

ctDNA, circulating tumour DNA; dMMR, DNA mismatch repair deficiency; pCR, pathologic complete response; PD, progressive disease; pMMR, proficient mismatch repair; TRG, tumour regression grading

INFINITY: SUMMARY

- Tremelimumab plus durvalumab (T300/D) for 3 months pre-operatively was safe and achieved promising eradicating activity in patients with resectable dMMR and MSI-H
- Chemo free ICI-based strategies have the potential to become standard of care in this molecular subgroup
- Enrolment in Cohort 2 is still ongoing after IDMC evaluation and protocol amendment to exclude cT4 tumours identified at baseline staging

Clinical takeaway:

- **Results from this study show potential of tremelimumab plus durvalumab as standard of care for patients with resectable MSI-H G/GEJ cancers**

cT, clinical T stage; dMMR, DNA mismatch repair deficiency; G/GEJ, gastric or gastroesophageal junction; ICI, immune checkpoint inhibitor; IDMC, Independent Data Monitoring Committee; MSI-H, microsatellite instability-high

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