Cetuximab, docetaxel, and cisplatin versus platinum, fluorouracil, and cetuximab as first-line treatment in patients with recurrent or metastatic head and neck squamous-cell carcinoma (GORTEC 2014-01 TPExtreme): a multicentre, open-label, randomised, phase 2 trial

Joël Guigay, Anne Aupérin*, Jérôme Fayette, Esma Saada-Bouzid, Cédrik Lafond, Miren Taberna, Lionnel Geoffrois, Laurent Martin, Olivier Capitain, Didier Cupissol, Hélène Castanie, Damien Vansteene, Philippe Schafhausen, Alison Johnson, Caroline Even, Christian Sire, Sophie Duplomb, Camille Evrard, Jean-Pierre Delord, Brigitte Laguerre, Sylvie Zanetta, Cécile Chevassus-Clément, Aldéric Fraslin, Fanny Louat, Laura Sinigaglia, Ulrich Keilholz†, Jean Bourhis†, Ricard Mesia†, on behalf of the GORTEC, AIO, TTCC, and UniCancer Head and Neck groups‡*

Study background

The TPExtreme study: Rationale for the study

Phase III EXTREME, 2008[1]

10.1 months mOS
Platinum + **5-FU*** + cetuximab

Improved outcomes, with no detriment to safety[1] or QoL[2]

Is it feasible to substitute 5-FU with a taxane and increase efficacy?

Phase II GORTEC, 2015[3]

14.0 months mOS
Cisplatin + **taxane*** + cetuximab†

The synergistic effect of taxanes + cetuximab has been demonstrated in preclinical studies[4]

+

Taxanes and cetuximab + platinum have shown promising anti-tumor efficacy†[3]

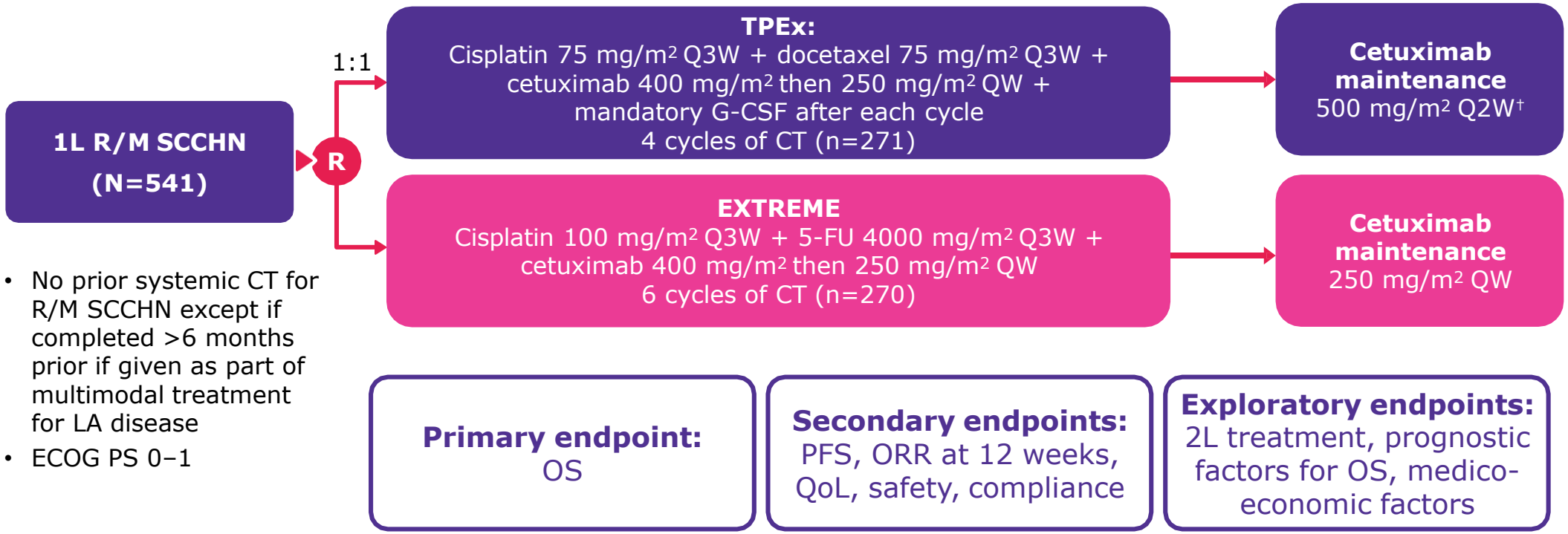
+

The TPEx regimen has advantages over EXTREME:‡[4,5]

- Shorter treatment infusion
- Easier delivery
- Fewer contraindications

*1. Vermorken JB, et al. N Engl J Med 2008;359:1116–1127; 2. Mesía R, et al. Ann Oncol 2010;21:1967–1973; 3. Guigay J, et al. Ann Oncol 2015;26:1941–1947;
4. Guigay J, et al. Front Oncol 2019;9:668; 5. Guigay J, et al. Lancet Oncol 2021;doi:S1470-2045(20)30755–5.

TPExtreme: The first large randomized study comparing TPEx with EXTREME for 1L R/M SCCHN[5]



- No prior systemic CT for R/M SCCHN except if completed >6 months prior if given as part of multimodal treatment for LA disease
- ECOG PS 0–1

Note: For the EXTREME arm, if cisplatin is not tolerated and/or when the total cumulative dose of cisplatin (including prior administration) reaches 600 mg/m², cisplatin has to be replaced with carboplatin, AUC 5.

5. Guigay J, et al. Lancet Oncol 2021;doi:S1470-2045(20)30755–5.

Baseline characteristics were well balanced between the arms[5]

Patient characteristics

	TPEx (n=269)	EXTREME (n=270)
Median age, years (range)	60 (55–64)	60 (55–63)
Male, n (%)	240 (89)	231 (86)
ECOG PS 1, n (%)	183 (68)	184 (68)
Current/former smoker, n (%)	255 (95)	243 (90)
Prior platinum, n (%)	156 (58)	140 (52)

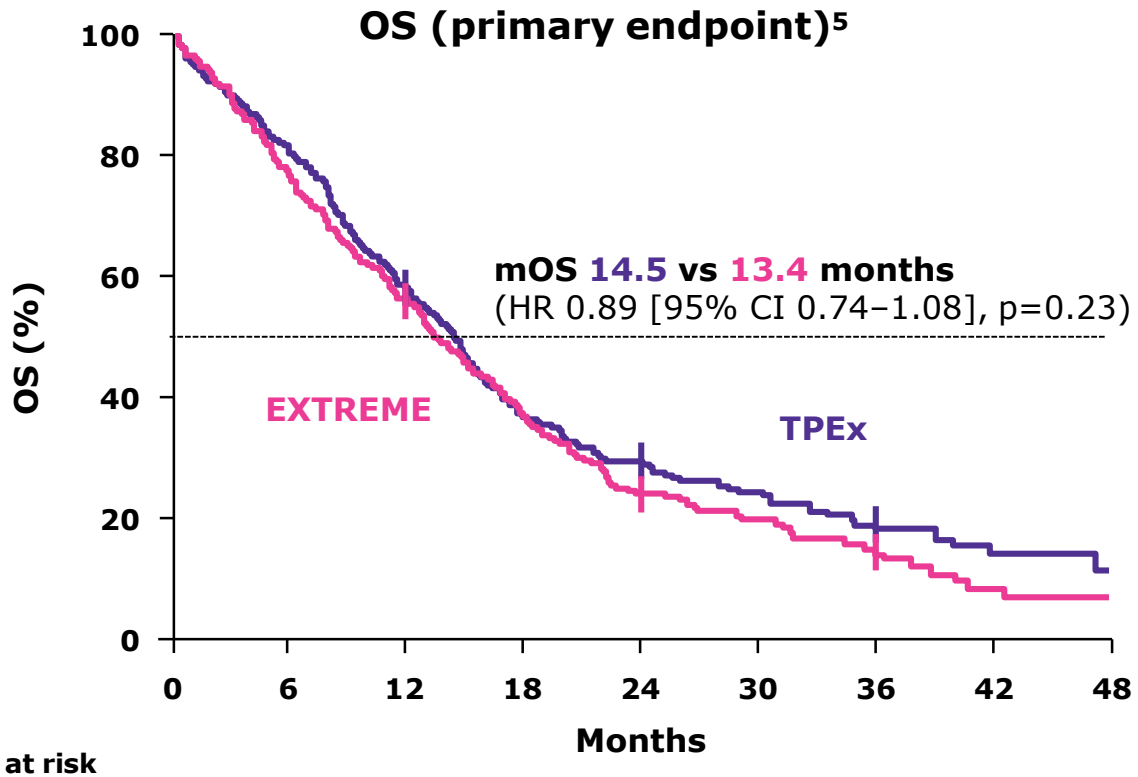
Disease characteristics

	TPEx (n=269)	EXTREME (n=270)
Primary tumor site		
Hypopharynx	54 (20%)	63 (23%)
Oral cavity	57 (21%)	52 (19%)
Larynx	34 (13%)	57 (21%)
Oropharynx (OPC)	120 (45%)	96 (36%)
OPC-HPV-DNA-positive	20/104 (19%)	14/76 (18%)
Type of disease at inclusion		
Metastatic alone	110 (41%)	118 (44%)
Locoregional relapse alone	94 (35%)	98 (36%)
Metastatic and locoregional relapse	65 (24%)	54 (20%)

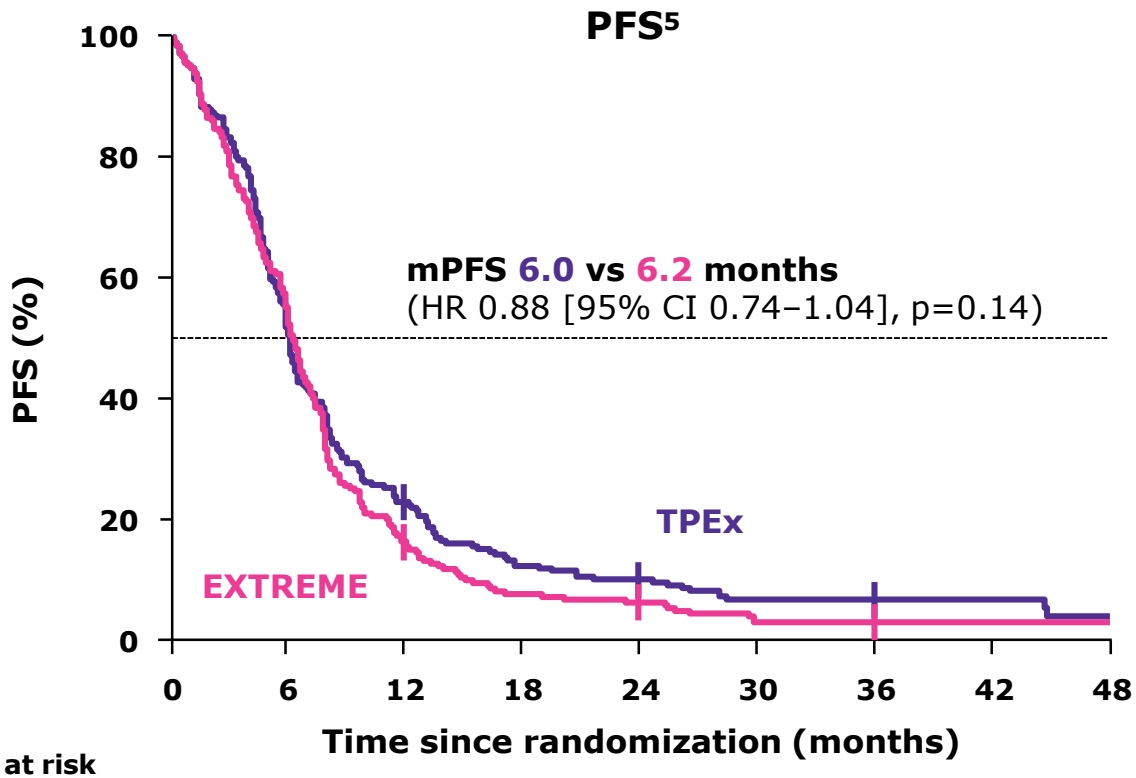
5. Guigay J, et al. Lancet Oncol 2021;doi:S1470-2045(20)30755–5.

Primary and secondary endpoints

The mOS for TPEx was similar to that of the EXTREME arm, which was higher than in any previous RCT*[1,4,5]



No. at risk									
TPEx	269	215	155	96	64	42	24	12	3
EXTREME	270	205	150	95	51	27	17	7	2



No. at risk									
TPEx	269	135	62	32	24	13	9	6	1
EXTREME	270	141	43	20	15	6	5	4	1

1. Vermorken JB, et al. New Engl J Med 2008;359:1116–1127; 4. Guigay J, et al. Front Oncol 2019;9:668; 5. Guigay J, et al. Lancet Oncol 2021;doi:S1470-2045(20)30755–5.

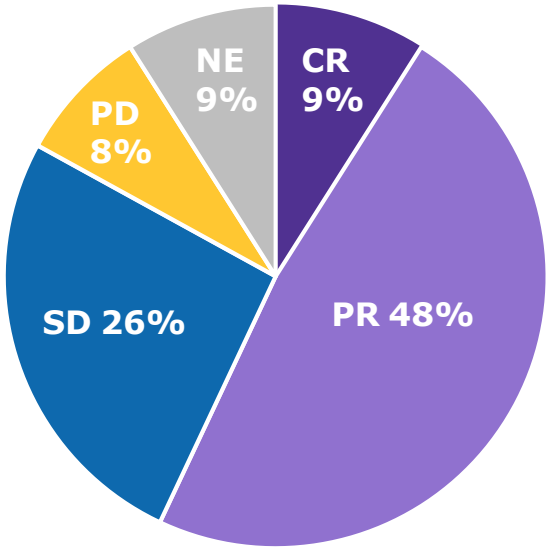
The TPEx and EXTREME regimens demonstrated similarly high response rates*[5]

ORR (Week 12, as per independent central review)[5]

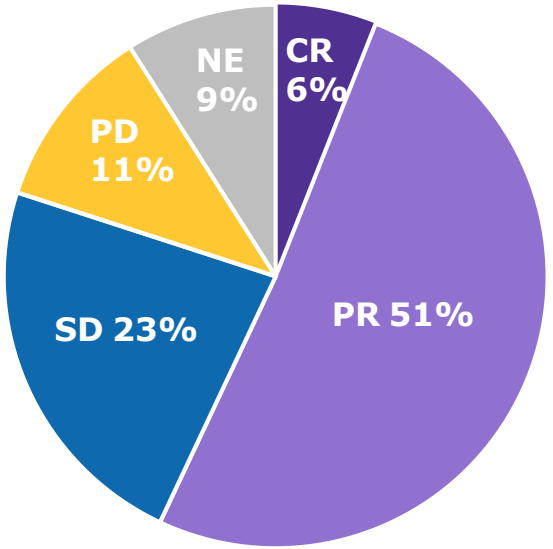
TPEx vs EXTREME:
57% vs **59%**, **p=0.64**

Best overall response (investigator-assessed)[5]

TPEx (n=269)

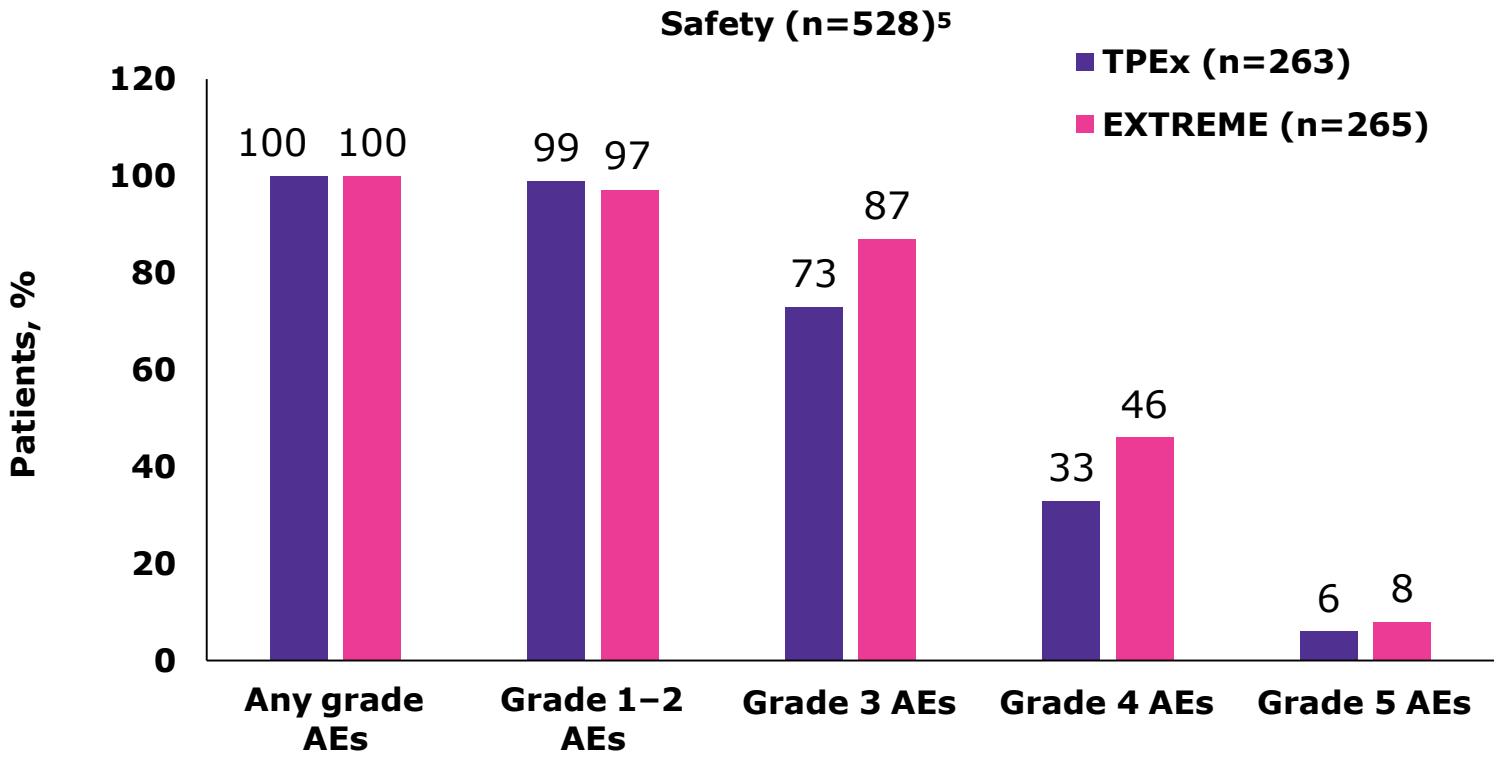


EXTREME (n=270)



5. Guigay J, et al. Lancet Oncol 2021;doi:S1470-2045(20)30755–5.

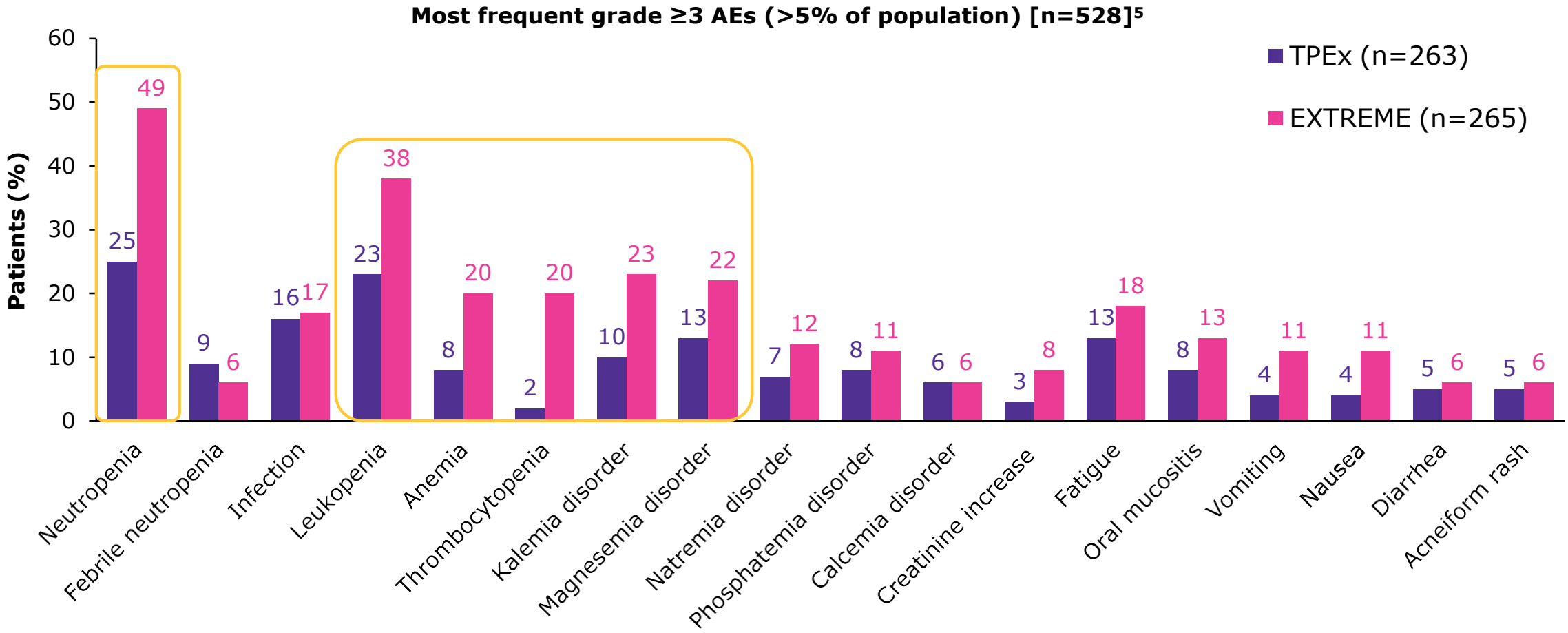
TPEx was associated with significantly fewer grade ≥3 AEs than EXTREME[5]



Total grade ≥3 AEs:
81% with TPEx
vs **93%** with EXTREME
(p<0.0001)[5]

5. Guigay J, et al. Lancet Oncol 2021;doi:S1470-2045(20)30755–5.

TPEx has a favorable safety profile compared with EXTREME[5]



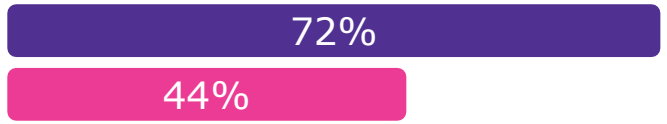
5. Guigay J, et al. Lancet Oncol 2021;doi:S1470-2045(20)30755–5.

Compliance to treatment was better with TPEx than with EXTREME[5]

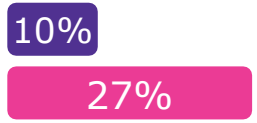
Compliance

Median number of CT cycles delivered, p:NR[5]

Patients who received all planned cycles of CT, p<0.0001[5]

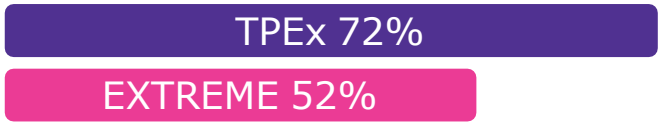


CT cycles administered with delay, p:NR[5]



Maintenance

Patients who started maintenance, p<0.0001[5]



Median duration of CT, p:NR[5]

Median duration of maintenance, p:NR[5]

5. Guigay J, et al. Lancet Oncol 2021;doi:S1470-2045(20)30755–5.

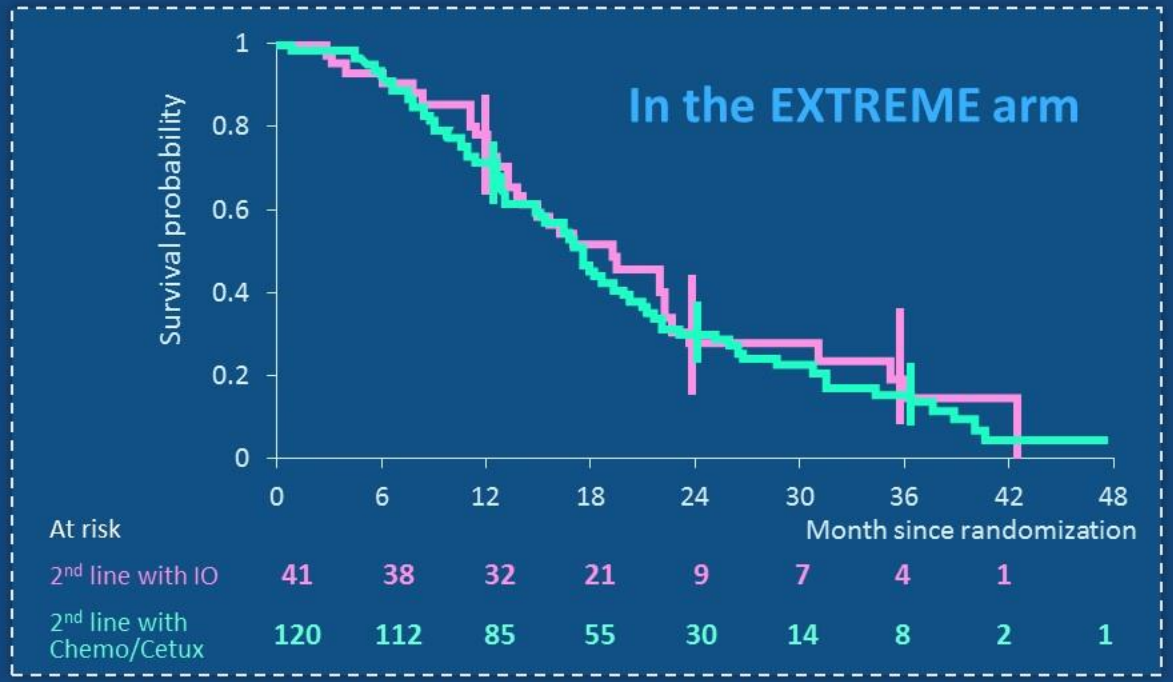
Exploratory endpoints

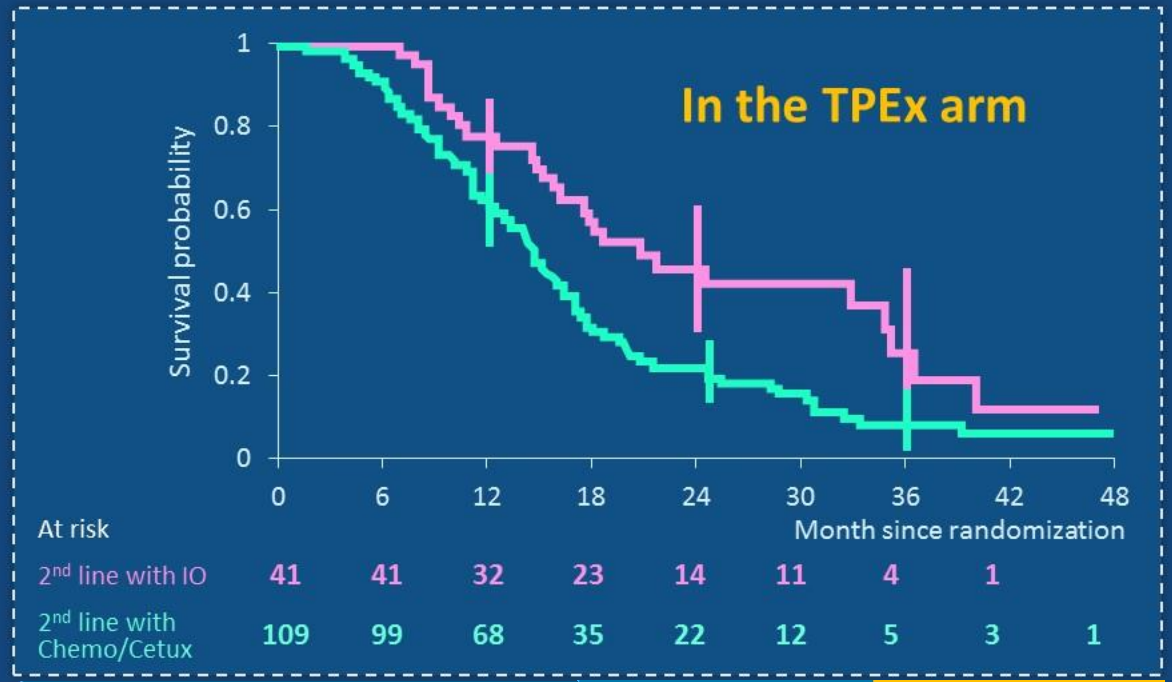
2nd line treatment

	EXTREME arm		TPEx arm	
Patients with 2nd line data available	256		245	
2nd line received	164 (64%)		157 (64%)	
Type of 2nd line				
IO (anti PD-1/PDL-1)	41 (16%)		41 (17%)	
Taxane based chemotherapy	56 (22%)	120 (47%)	30 (12%)	109 (44%)
Other chemotherapy	40 (16%)		61 (25%)	
Cetuximab +/- chemotherapy	24 (9%)		18 (7%)	
Radiotherapy	3 (1%)		7 (3%)	

- 79% and 85% of the 2nd line treatments were given after progression in EXTREME and TPEx arms, respectively.

2nd line treatment: Overall Survival since randomization in each arm according to Chemo +/- Cetux vs IO





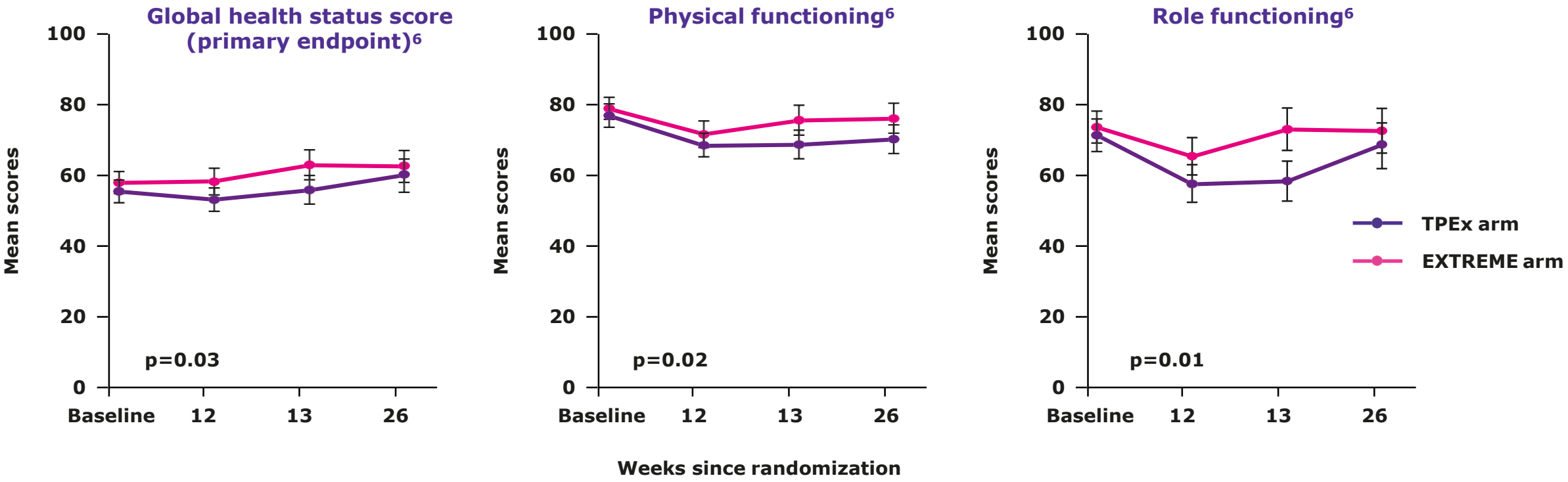
Median OS (95%CI)	**17.6 months (15.2 – 19.5)**	**19.4 months (13.4 – 22.3)**

Median OS (95%CI)	**14.9 months (13.0 – 16.3)**	**21.9 months (15.9 – 35.0)**

Significantly improved QoL scores were observed with TPEx vs EXTREME*[1,6]

Pre-specified exploratory analysis of QoL[5]

The EORTC QLQ-C30 was used to measure patient QoL at baseline, Weeks 12, 18, and 26



5. Guigay J, et al. Lancet Oncol 2021;doi:S1470-2045(20)30755–5; 6. Guigay J, et al. Lancet Oncol 2021;doi:S1470-2045(20)30755–5 (Supplementary appendix).

The large, randomized TPExtreme study: Summary*

The TPExtreme study compared TPEx (cisplatin + docetaxel + cetuximab) with EXTREME (platinum + 5-FU + cetuximab), both followed by cetuximab maintenance, for the treatment of 1L R/M SCCHN[5]

Compared with EXTREME, the TPEx regimen offered simplified dosing and administration, and required fewer cycles of CT (4 vs up to 6)[5]

As the TPEx regimen does not contain 5-FU, it is suitable for patients with DPD deficiency[8]

Treatment with TPEx was associated with robust OS, PFS and ORR outcomes, with low levels of PD[5]

TPEx demonstrated improved safetyand compliance vs EXTREME[5]

TPEx demonstrated improved QoL outcomes vs EXTREME, with improvements in global health status, and physical and role functioning[5]

Treatment with 1L TPEx, followed by 2L ICI, resulted in an unprecedented, long mOS of 21.9 months[5,6]

TPEx is a SoC treatment option, recommended by international guidelines for the treatment of

1L R/M SCCHN[8]

5. Guigay J, et al. Lancet Oncol 2021;doi:S1470-2045(20)30755–5; 6. Guigay J, et al. Lancet Oncol 2021;doi:S1470-2045(20)30755-5 (Supplementary appendix);
8. Machiels JP et al. Ann Oncol 2020;31:462–1475.