ORL

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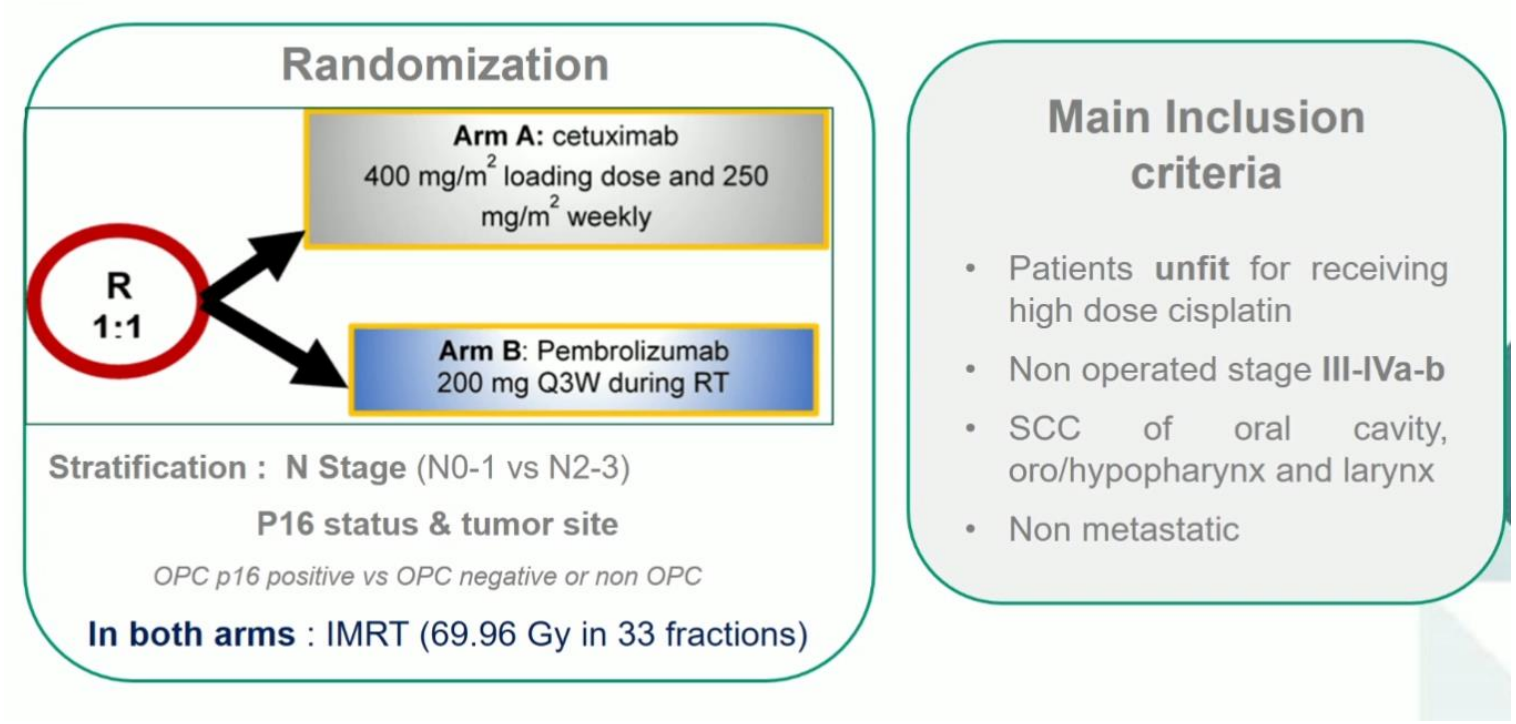
Pembrorad: rtt+ cetuximab vs rtt+ pembrolizumab patient unfit cisplatine



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Pembrorad: rtt+ cetuximab vs rtt+ pembrolizumab patient unfit cisplatine

May 2016 - Oct. 2017: **133** pts randomized: 66 Cetux-RT, 67 Pembro-RT

All characteristics well balanced between two arms

Patients Characteristics

	Cetux-RT N=65		Pembro-RT N=66	
	N	%	N	%
Age (years)	Median: 67 [47 – 81]		Median: 65 [48 – 79]	
PS (ECOG)				
0	24	37	27	41
1	41	63	39	59
Tobacco				
Never smoker	6	9	4	6
Former smoker	37	57	37	56
Current smoker	22	34	25	37
Tumor site				
Oropharynx	40	62	39	59
Oral cavity	5	8	4	6
Hypopharynx	11	17	18	27
Larynx	9	14	5	8
Stage				
III	17	26	16	24
IVa	40	62	33	50
IVb	8	12	17	26

- 75% ont reçu au moins 7 cycles de cetuximab
- 88% ont reçu au moins 3 cycles de pembrolizumab

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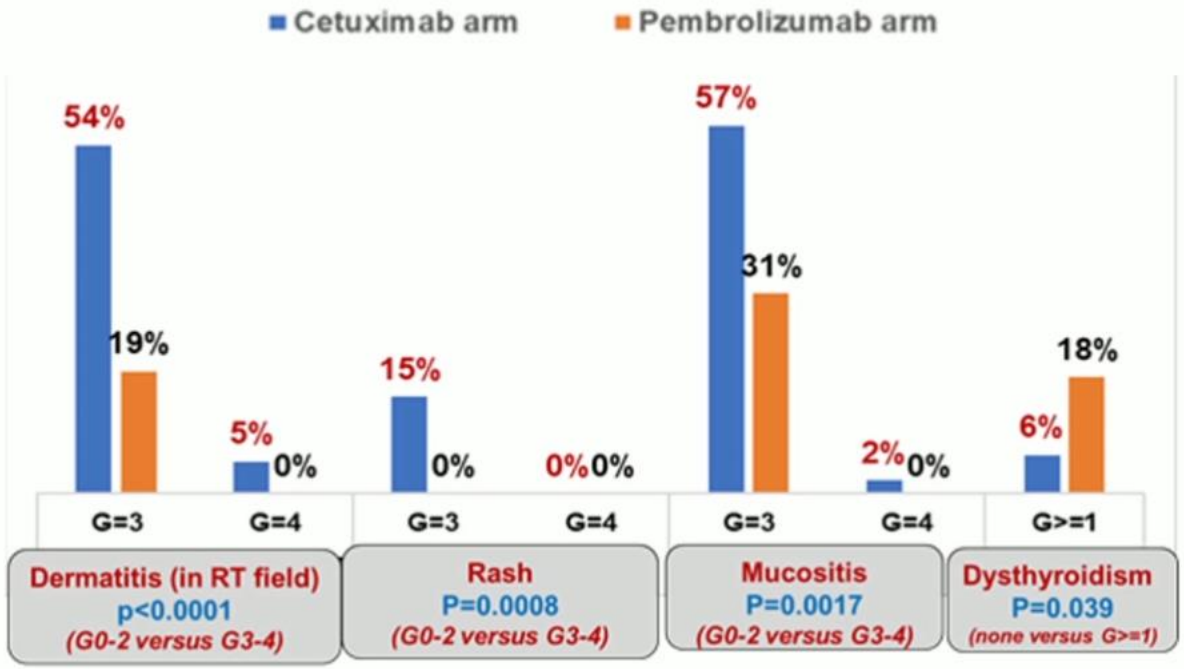

- Significantly higher rate of AE **G>=3: radio-dermatitis**, **rash** and **mucositis** in **Cetux-RT** arm than in Pembro-RT
- **G>=1 Dysthyroidism** was more frequent in **Pembro-RT** arm than in Cetux-RT

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Primary endpoint

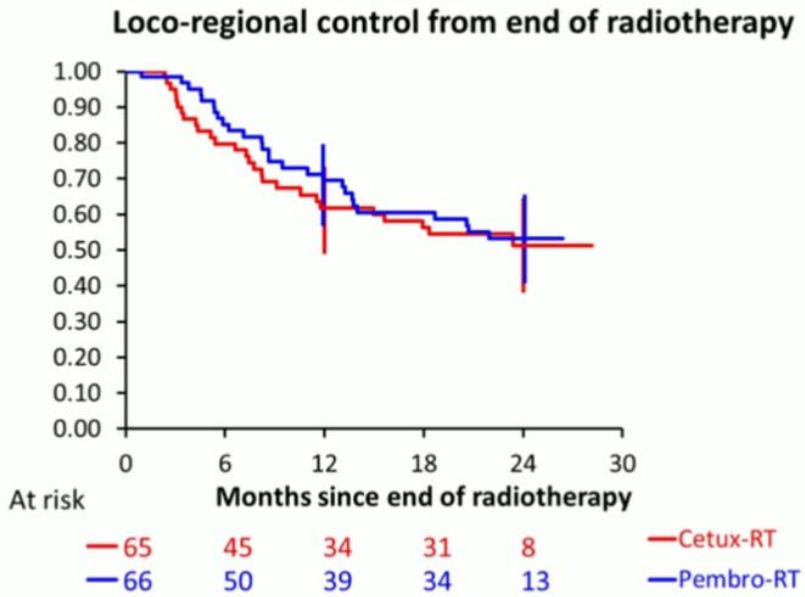
Loco-regional control at 15 months after radiotherapy

- **Median Follow-up: 25.6** months (9.0-30.2 months)
- **LRC at 15 months after RT:**

Cetux-RT : 59% (95%CI 45%-72%)

Pembro-RT : 60% (95%CI 46%-72%)

OR = 1.05, (95%CI 0.43-2.59); **p = 0.91**



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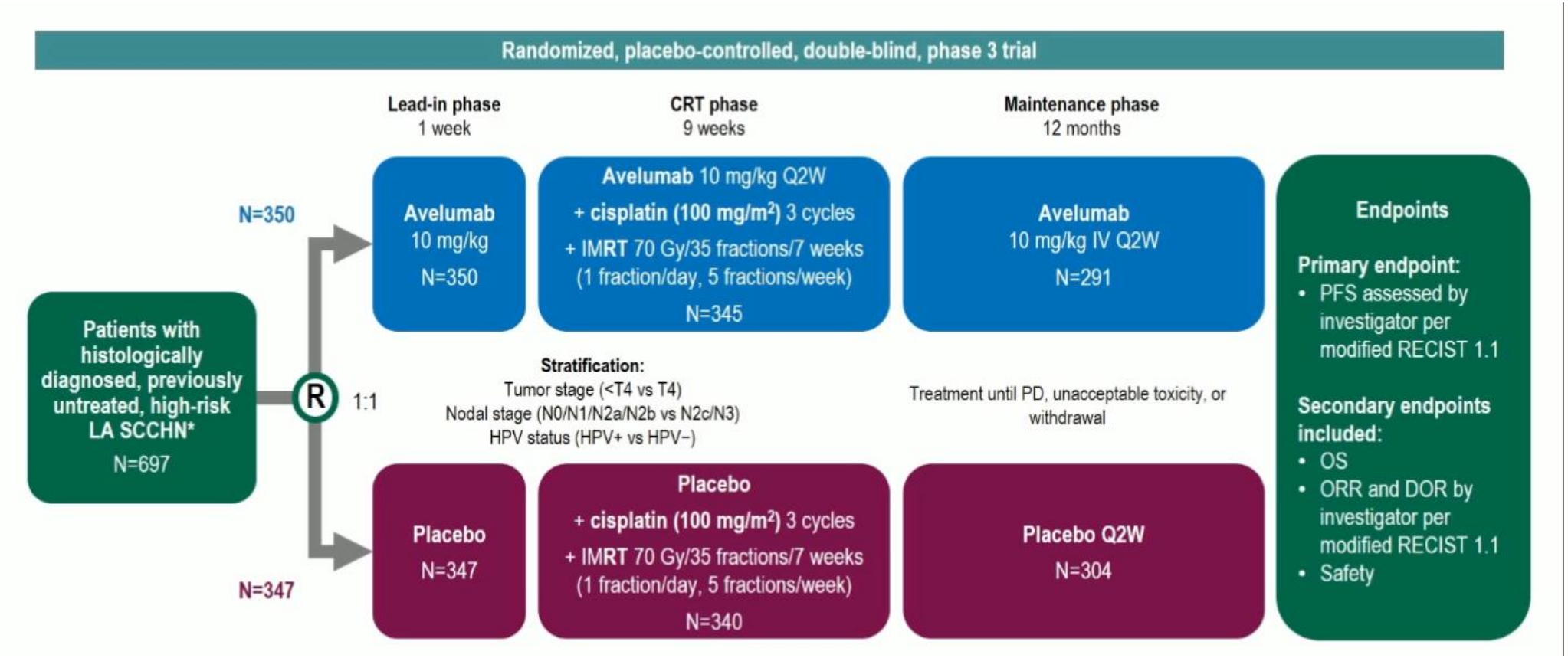
Javelin 100: rtt-chimio +/- avelumab: phase 3



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Javelin 100: rtt-chimio +/- avelumab: phase 3

Baseline characteristics

	Avelumab + CRT (n=350)	Placebo + CRT (n=347)
Age, median, years	60	59
Sex, %		
Male	83	82
Female	17	18
ECOG performance status, %		
0	55	62
1	45	38
Geographic region, %		
North America	23	27
Western Europe	30	33
Eastern Europe	15	13
Asia	29	24
Rest of the world	3	4

	Avelumab + CRT (n=350)	Placebo + CRT (n=347)
Site of primary tumor, %		
Oral cavity	13	14
Oropharynx	45	49
Larynx	17	19
Hypopharynx	25	18
HPV status, %*		
Positive	35	34
Negative	65	66
Tumor stage at baseline, %†		
<T4	57	56
T4	43	44
Nodal stage at baseline, %†		
N0/N1/N2a/N2b	53	52
N2c/N3	47	48

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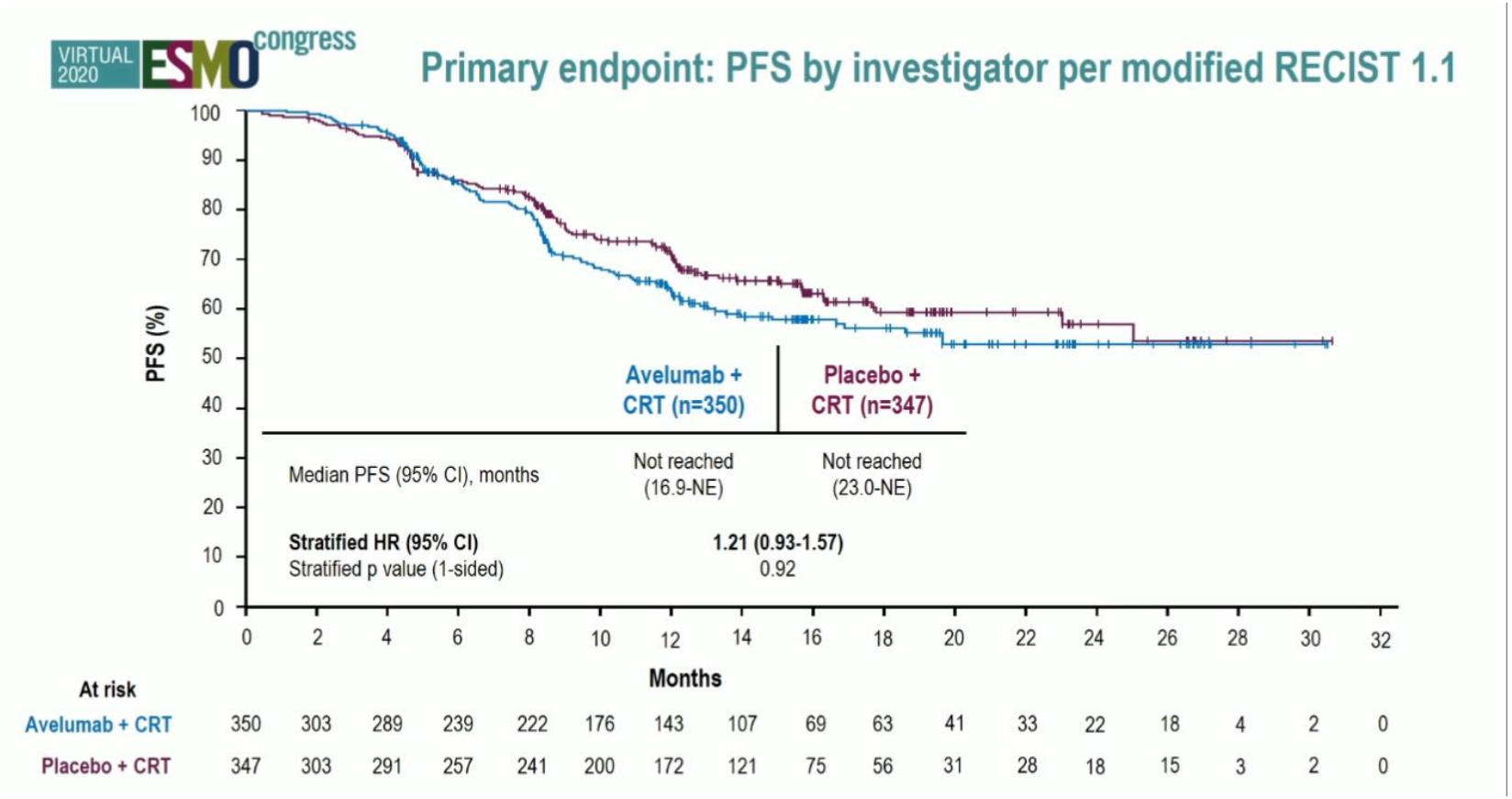

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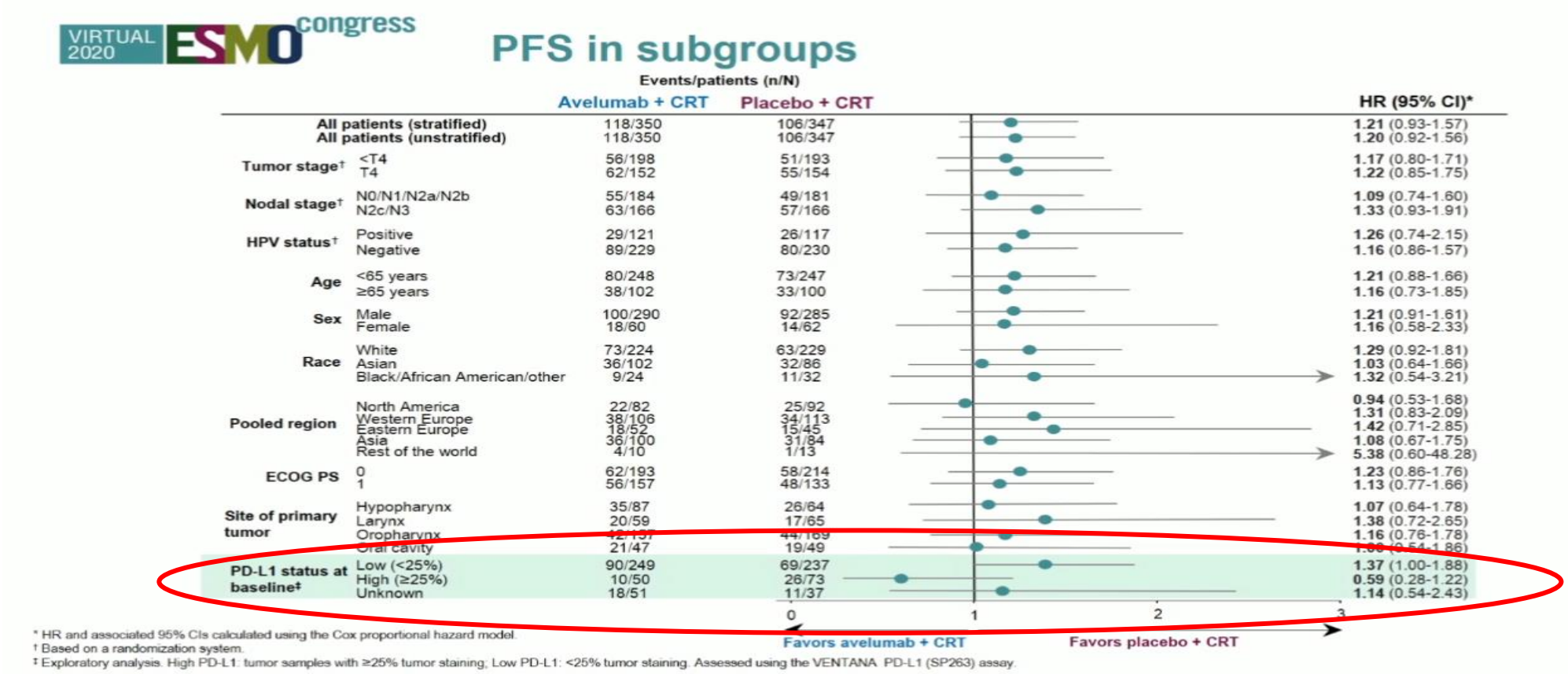

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Javelin 100: rtt-chimio +/- avelumab: phase 3

	Avelumab + CRT (n=348)		Placebo + CRT (n=344)	
	All grades	Grade 3/4	All grades	Grade 3/4
Any TRAE, %*	**98**	**66/14**	**99**	**63/11**
Nausea	55	6	55	5
Anemia	53	12	50	13
Dry mouth	42	1	43	1
Mucosal inflammation	41	14	37	13
Radiation skin injury	39	5	40	5
Dysphagia	38	14	40	14
Weight decreased	35	4	43	6
Decreased appetite	33	7	33	5
Dysgeusia	30	0	34	1
Neutropenia	30	16	28	15
Fatigue	29	4	34	3
Vomiting	28	5	31	6
Stomatitis	27	7	28	8
Blood creatine increased	22	2	20	1
Hypomagnesemia	22	1	18	1
Neutrophil count decreased	18	11	17	9
Oropharyngeal pain	18	3	23	2
Infusion-related reaction, %	22	2	3	<1

TRAE, treatment-related adverse event.
* TRAEs of any grade occurring in ≥20% of patients or grade 3/4 in ≥10% patients. Two patients died in the avelumab arm (death and vascular rupture; n=1 each) and 1 patient in the placebo arm (acute respiratory failure).

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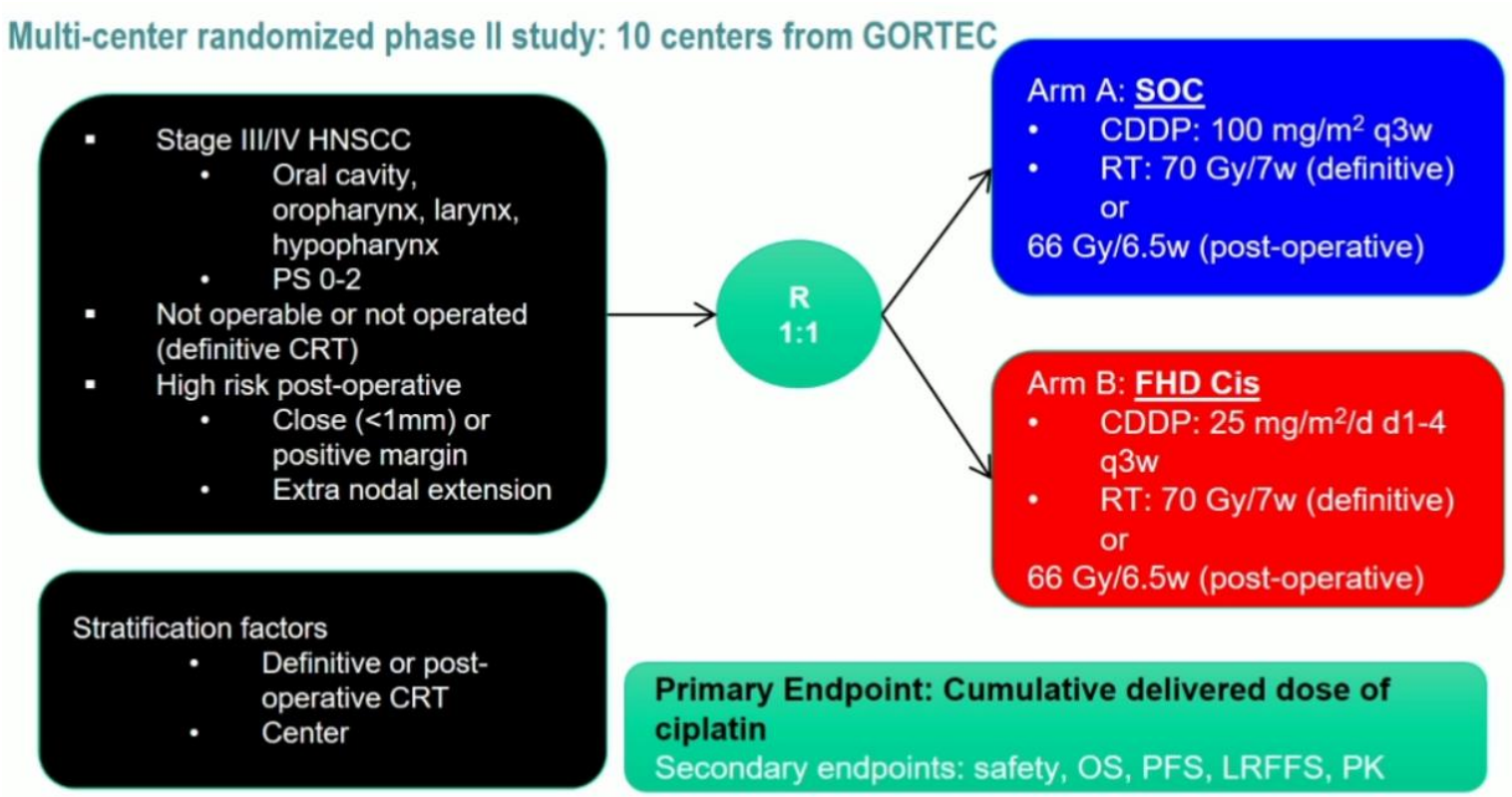
Conclusion

- Pas d'efficacité des immunothérapies en association avec la radiothérapie
- Bon profil de toxicité

- Place de l'adjuvant?? (pembrorad)
- PD-1 vs PDL-1??
- Sélection des patients (PDL-1)

Results of the GORTEC 2015-02 CisFRad randomized trial



Cisplatin mg/m²	SOC (100)	FHD Cis (25X4)	p
Nb of Patients	65	59	
Median	280	291	
Q1	199	256	0.03*
Q3	295	298	

* Wilcoxon non parametric test

3 cycles: 84% FHD Cis vs 67% SOC

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Cis-Frad: Toxicité

Any grade: n(%)	SOC	FHD Cis	p
Renal imp.	20 (35)	14 (26)	0.30
Hearing imp.	12 (23)	6 (12)	0.14

SAEs: 32 with SOC vs 19 with FHD CIS
P = 0.07

Grade III-IV toxicities		SOC	FHD Cis	p
CDDP related	Neutropenia	14	5	0.03
	Anemia	8	0	0.006
	Thrombocyt.	2	0	NS
	Renal imp.	2	1	NS
	Na	2	0	NS
	K	2	0	NS
	Mg	1	0	NS
	Albumine	1	0	NS
	Transaminase	1	0	NS
	Hearing imp.	2	0	NS
	Nausea	3	3	NS
CRT related	Mucositis	14	12	NS
	Dysphagia	19	17	NS
	Cutaneous	11	4	0,07
	Sepsis	9	8	NS
TOTAL		91	50	<0.001

Conclusions

- Dose cumulée supérieure avec le fractionné
- Moins de toxicité
- Pas de différence sur l'efficacité
- Option possible

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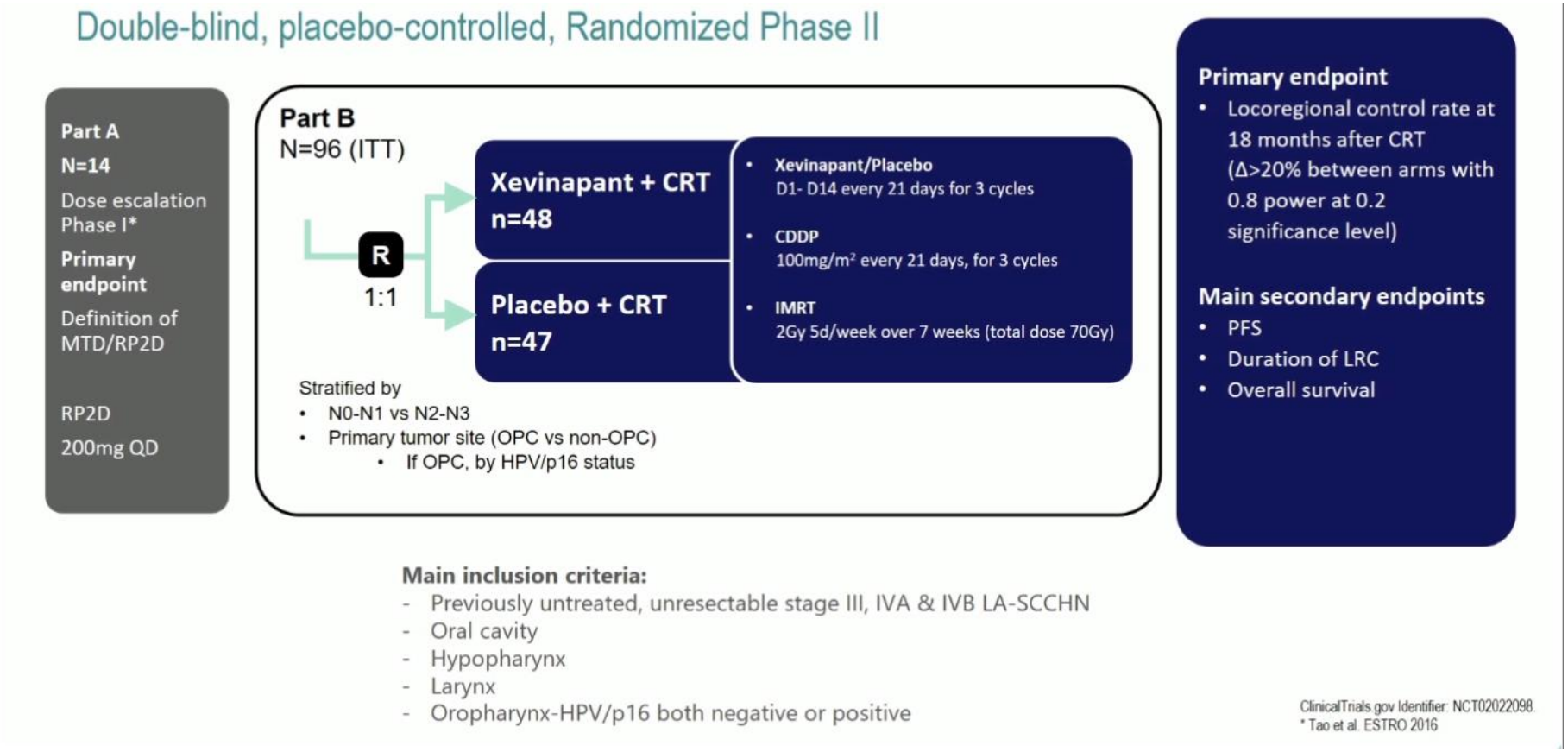
Debio-1143 (Xevinapant) plus radio-chimiothérapie: résultat à 3 ans



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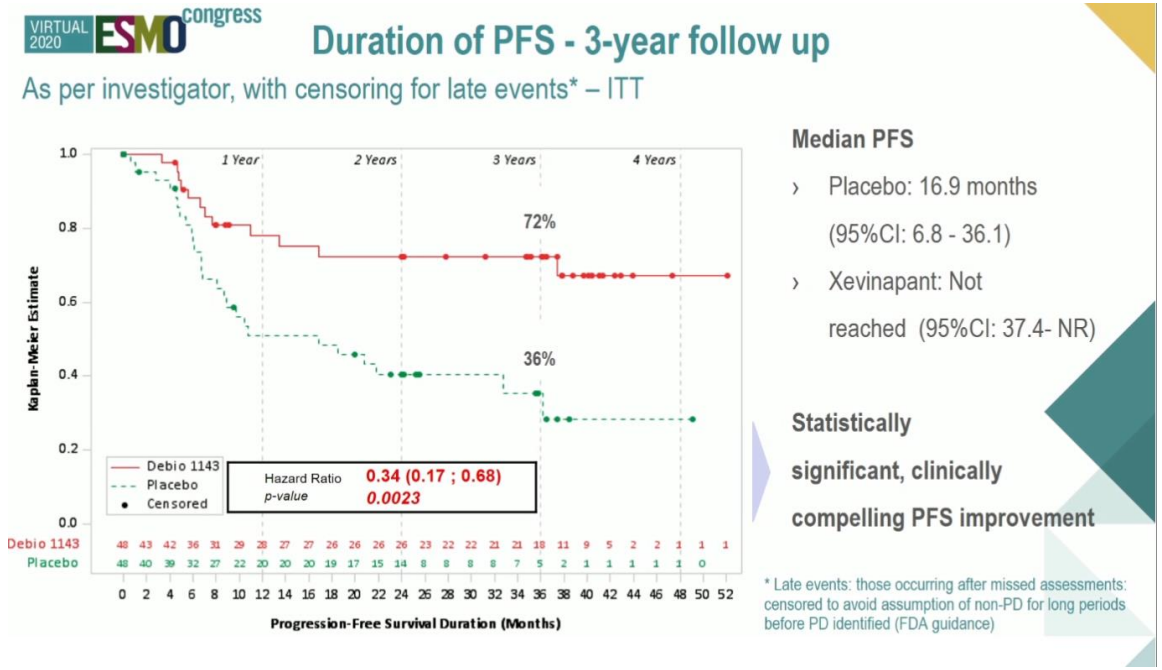
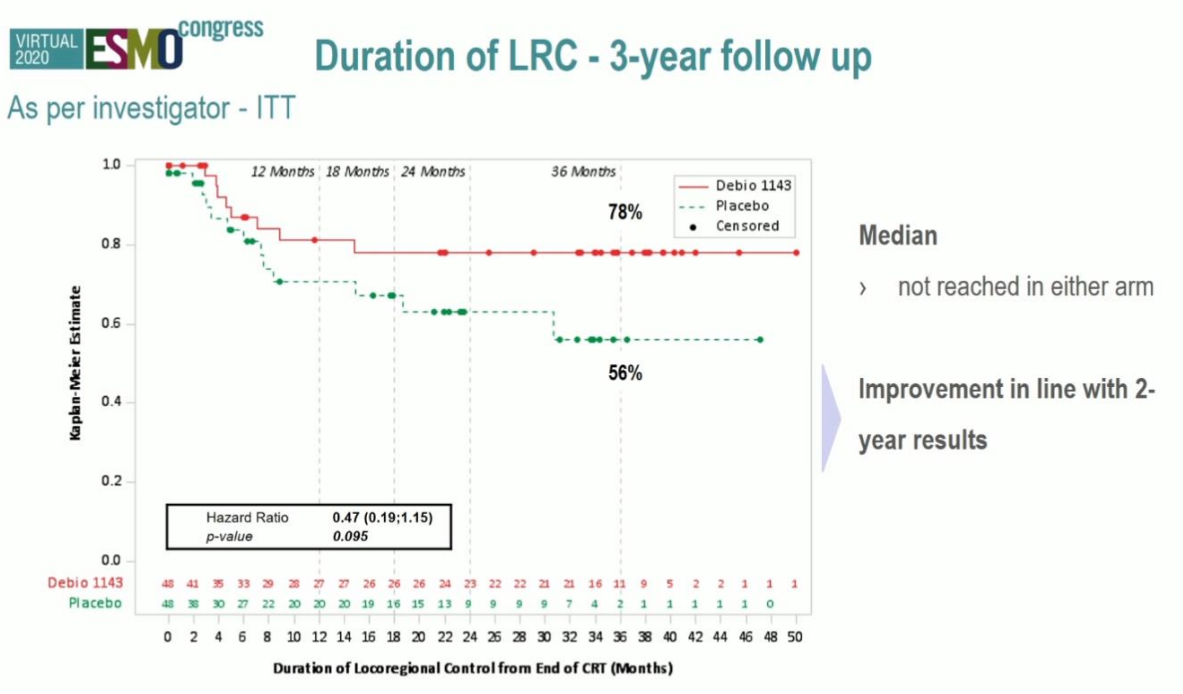
Debio-1143 (Xevinapant) plus radio-chimiothérapie: résultat à 3 ans





- Update de l'ASCO
- Résultat encourageant +++, à confirmer par phase 3

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