2021 ESMO congress

JUPITER-06:

A Randomized, Double-blind, Phase 3 Study of Toripalimab versus Placebo In Combination with First-Line Chemotherapy for Treatment Naive Advanced or Metastatic Esophageal Squamous Cell Carcinoma (ESCC)

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Presented by Feng Wang MD, PhD at 2021 ESMO Annual Meeting

DECLARATION OF INTERESTS

Feng Wang MD, PhD

No conflicts of interest

Rui-Hua Xu MD, PhD

Consulting or Advisory Role:

Bristol-Myers Squibb, Merck Serono, Roche, Astellas, and AstraZeneca.

Resume

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- Profile:

Dr. Feng Wang is currently a professor and vice director in the Department of Medical Oncology at Sun Yat-Sen University Cancer Center, Guangzhou, China. She has extensive experience and expertise in the field of Gastrointestinal Medical Oncology and translation research in gastrointestinal cancers. Dr Wang sees more than 3 thousand patients with gastrointestinal cancers annually and has initiated or participated in many investigator initiated and NMPA approved clinical trials. She presides over a number of research programs including the international (regional) cooperation and exchange program, and general program from the national natural science foundation of China, the Doctoral Program of Higher Education of China, and has participated in several international cooperation, national and provincial level projects. Dr. Wang has published over 90 peer-reviewed articles, including some first author or corresponding author papers in renowned journals such as JAMA Oncology, Cell Research, Annals of Oncology, EMBO Mol Med, Oncogene, etc and has been invited to present her research results at AACR, CSCO, Nature Conference, Chinese Congress of Oncology and other international conferences. She was awarded many prizes including the Second Prize of National Science and Technology Progress Award, First Prize of Chinese Medical Science and Technology Award, the First Prize of Guangdong Province Science and Technology Progress Award, the Outstanding Young Talents of Sun Yat-sen University Cancer Center and the New Stars of Science and Technology in Guangzhou etc. She holds many academic posts, including the vice director of Youth Committee of Professional Committee of Tumor Targeted Therapy, Chinese anti-cancer association and a Chairing Committee member of Chinese Society of Clinical Oncology etc.

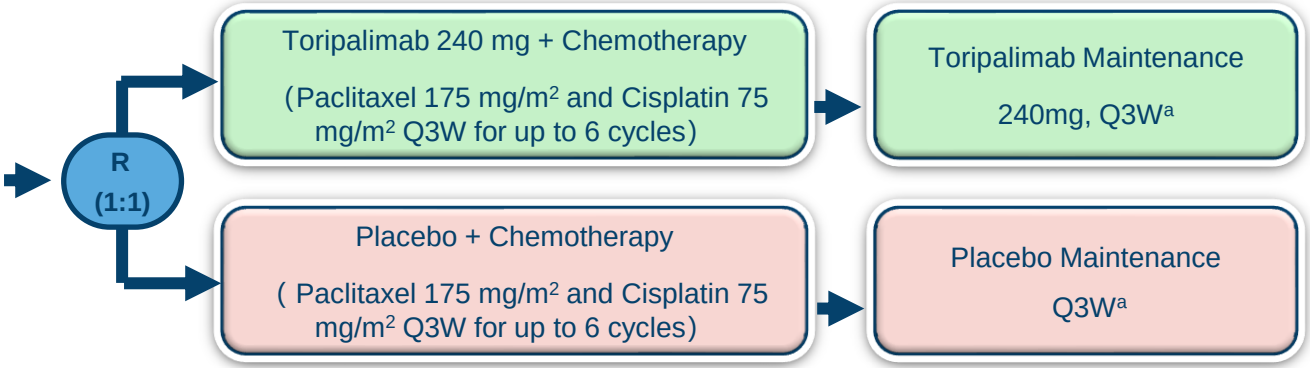
JUPITER-06 : Study Design

Key Eligibility Criteria

- Histologically or cytologically confirmed advanced or metastatic ESCC
- Treatment-naïve for metastatic disease
- ECOG PS of 0 or 1
- Measurable disease per RECIST v1.1

Stratification Factors

- Prior Radiation (yes vs no)
- ECOG PS 0 vs 1



- Co-Primary endpoints: PFS by BICR per RECIST v1.1 and OS
- Secondary endpoints: PFS by the Investigator, ORR , DoR , DCR, and 1-year and 2-year PFS & OS rates, safety, and HRQoL

[a] Until progressive disease, intolerable toxicity, withdrawal of consent or investigator's judgement or a maximum treatment of 2 years.

Abbreviation: RECIST, Response Evaluation Criteria in Solid Tumors; ECOG PS, Eastern Cooperative Oncology Group performance status score; BICR, blind independent central review ; IV, intravenously; PFS, progression-free survival; OS, overall survival; ORR, objective response rate; DCR, disease control rate; DoR, duration of response; HRQoL, health-related quality of life.

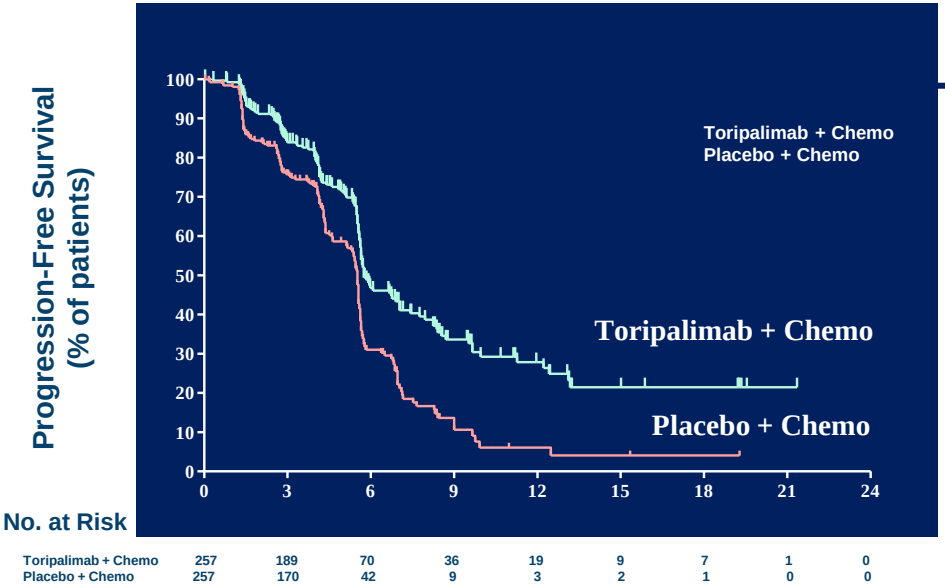
Baseline Characteristics

Characteristic	Toripalimab + chemotherapy	Placebo + chemotherapy
	N=257; n (%)	N=257; n (%)
Median age (range),years	63.0 (20-75)	62.0 (40-74)
≥65 years	101 (39.3)	94 (36.6)
Male	217 (84.4)	220 85.6)
Previous radiation therapy	35 (13.6)	34 (13.2)
ECOG PS 1	191(74.3)	192 (74.7)
Disease status		
Recurrent or unresectable	50(19.5)	59 (23.0)
Metastatic	206 (80.2)	198 (77.0)
Not available	1(0.4)	0
PD-L1 expression		
CPS<1	43 (16.7)	44 (17.1)
CPS≥1	201 (78.2)	200 (77.8)
CPS<10	129 (50.2)	147 (57.2)
CPS≥10	115 (44.7)	97 (37.7)
Unknown	13 (5.1)	13 (5.1)

Data cut-off date: 22/Mar/2021

Progression-Free Survival by BICR per RECIST v1.1

Final PFS Analysis Data cut-off Date: Mar 22, 2021



No. of Events/ Total No. of Patients	Median Progression-free Survival, months (95% CI)	1-Yr Progression-free Survival Rate, % (95% CI)
132/257	**5.7 (5.6, 7.0)**	**27.8 (20.4, 35.8)**
164/257	5.5 (5.2, 5.6)	6.1 (2.2, 12.6)

Stratified HR for disease progression or death,

0.58 (95% CI 0.461, 0.738);
P<0.00001

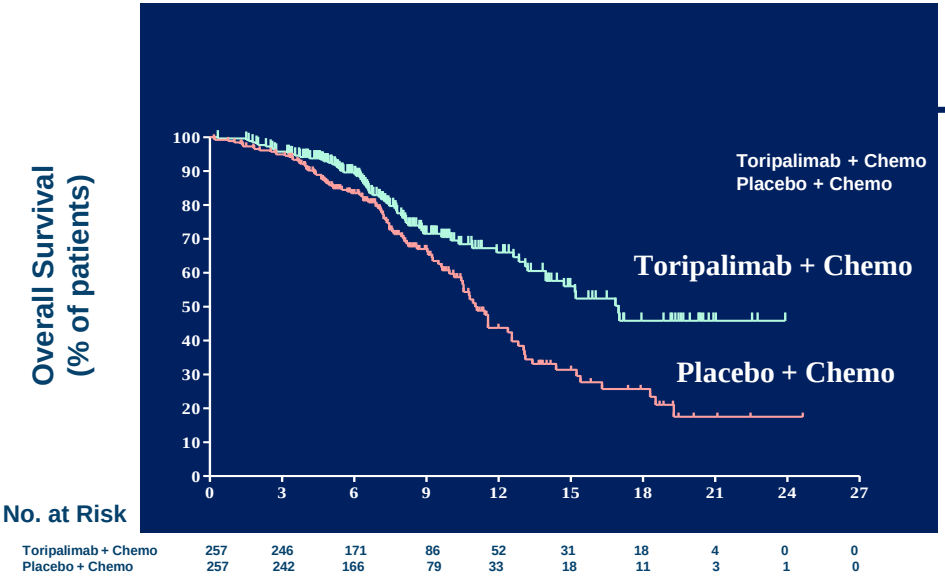
PD-L1 expression subgroups:

CPS ≥ 1: 5.7 vs. 5.5 months, HR=0.58 (95%CI 0.444, 0.751)

CPS < 1: 5.7 vs. 5.6 months, HR=0.66 (95%CI 0.370, 1.189)

Overall Survival

Interim OS Analysis Data cut-off Date: Mar 22, 2021



No. of Deaths/ Total No. of Patients	Median Overall Survival (95% CI) *mo*	1-Yr Overall Survival Rate % (95% CI)	2-Yr Overall Survival Rate % (95% CI)
70/257	**17.0 (14.0, NE)**	**66.0 (57.5, 73.2)**	**NE (NE, NE)**
103/257	11.0 (10.4, 12.6)	43.7 (34.4, 52.6)	17.5 (8.7, 28.9)

Stratified HR for death,

0.58 (95% CI 0.425, 0.783);
P=0.00036

PD-L1 expression subgroups:

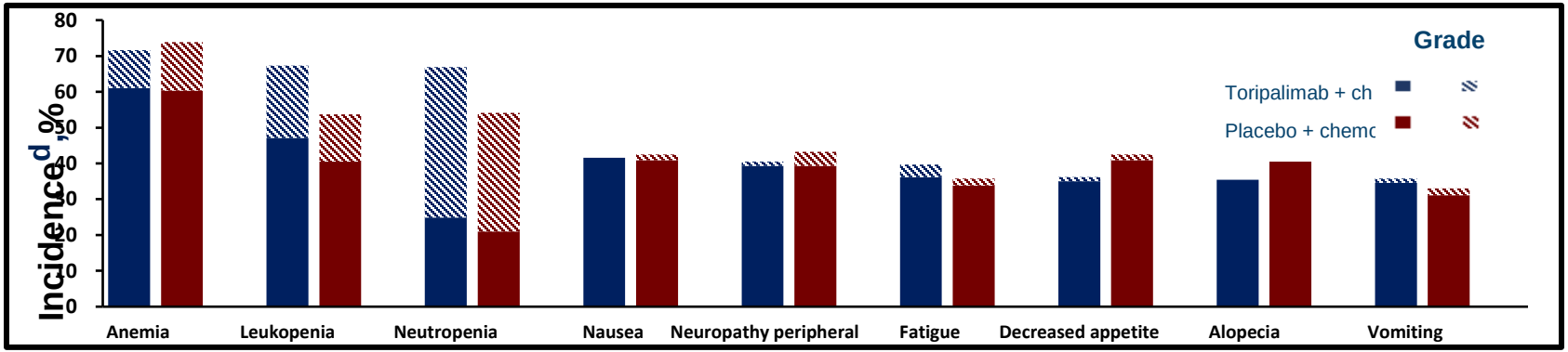
CPS ≥ 1: 15.2 vs. 10.9 months, HR=0.61 (95%CI 0.435, 0.870)

CPS < 1: NE vs. 11.6 months, HR=0.61 (95%CI 0.297, 1.247)

Presented by Feng Wang, MD, PhD

Safety Overview

Patients[a], n (%)	Toripalimab + chemotherapy (N=257)		Placebo + chemotherapy (N=257)	
	Any grade	Grade≥3	Any grade	Grade≥3
Any TRAEs[b,c]	250 (97.3)	166 (64.6)	250 (97.3)	144 (56.0)
Immune-related AEs [c]	95 (37.0)	18 (7.0)	68 (26.5)	4 (1.6)
leading to discontinuation	9 (3.5)	7 (2.7)	2 (0.8)	1 (0.4)
Infusion reactions	9 (3.5)	2 (0.8)	8 (3.1)	0
Fatal AEs	1 (0.4)	1 (0.4)	3 (1.2)	3 (1.2)



[a] Patients received at least 1 dose of the study drug.; [b] TRAE=Treatment related adverse events; [c] Based on investigator's assessment.
[d] TRAEs with ≥30% incidence in any treatment arm; Data cut-off date: Mar 22, 2021.

Summary

- The addition of toripalimab to paclitaxel+ cisplatin (TP) as a first-line treatment for advanced or metastatic ESCC patients provided superior PFS and OS than TP chemotherapy alone. PFS and OS benefits were observed in all key subgroups, including PD-L1 expression subgroups.
  - PFS：median 5.7 vs. 5.5 months, HR=0.58 (95%CI: 0.461, 0.738), P<0.00001
  - OS：median 17.0 vs. 11.0 months, HR=0.58 (95%CI: 0.425, 0.783), P =0.00036
- No new safety signals were identified with toripalimab added to chemotherapy
- Toripalimab in combination with TP chemotherapy has the potential to become a new standard first-line therapy in patients with advanced or metastatic ESCC.

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