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Adjuvant cemiplimab for high-risk cutaneous squamous cell carcinoma: Evaluating dosing intervals in a phase III trial

D. Rischin[1], S. Porceddu[2], F. Day[3], H. Christie[4], J.E. Jackson[5], B. Stein[6], Y.B. Su[7], R. Ladwa[8], N. Yamazaki[9], P. Bossi[10], A. Challapalli[11], A. Hauschild[12], F.A. Seebach[13], F. Cardozo[14], S-Y. Yoo[15], H. Ju[16], S. Bansal[17], P. Goncalves[18], M. Fury[19], J. Visich[20]

[1] Medical Oncology, Peter MacCallum Cancer Centre, Melbourne, Australia, [2] Department of Radiation Oncology, Peter MacCallum Cancer Centre, Melbourne, Australia, [3] Medical Oncology, Calvary Mater Newcastle, Waratah, Australia, [4] Medical Oncology, Cancer Care Centre Hervey Bay, Urraween, Australia, [5] Radiation Oncology, Radiation Oncology Centers, Gold Coast, Australia, [6] Medical Oncology, ICON Cancer Centre Adelaide (Kurralta Park), Adelaide, Australia, [7] Head and Neck Medical Oncology, Nebraska Cancer Specialists, Omaha, United States of America, [8] Medical Oncology, Princess Alexandra Hospital - Metro South Health, Woolloongabba, Australia, [9] Dermatologic Oncology, National Cancer Center - Tsukiji Campus, Chuo-ku, Japan, [10] Medical Oncology, IRCCS Humanitas Research Hospital, Rozzano, Italy, [11] Bristol Cancer Institute, University Hospitals Bristol & Weston NHS Foundation Trust, Bristol, United Kingdom, [12] Dermatology, Venereology and Allergology, UKSH - Universitätsklinikum Schleswig-Holstein - Campus Kiel, Kiel, Germany, [13] Oncology and Translational Sciences, Regeneron Pharmaceuticals, Inc., Tarrytown, United States of America, [14] Quantitative Pharmacology, Regeneron Pharmaceuticals, Inc., Tarrytown, United States of America, [15] Biostatistics Dept., Regeneron Pharmaceuticals, Inc., Tarrytown, United States of America, [16] Global Patient Safety, Regeneron Pharmaceuticals, Inc., Tarrytown, United States of America, [17] Clinical Oncology & Translational Sciences, Regeneron Pharmaceuticals, Inc., Tarrytown, United States of America, [18] Oncology, Regeneron Pharmaceuticals, Inc., Tarrytown, United States of America, [19] Oncology Clinical Sciences, Regeneron Pharmaceuticals, Inc., Tarrytown, United States of America[20] Clinical Pharmacology, Regeneron Pharmaceuticals, Inc., Tarrytown, United States of America

Background

Cemiplimab is the first adjuvant systemic therapy to improve disease-free survival (DFS) compared with placebo for patients with high-risk cutaneous squamous cell carcinoma (CSCC; HR 0.32). Here we present pharmacokinetic (PK) and safety data for two regimens of cemiplimab in patients with high-risk CSCC.

Methods

In this double-blind, placebo-controlled study, the primary endpoint was DFS. Secondary endpoints included safety, steady-state PK and immunogenicity.

Results

A total of 209 patients were randomised to cemiplimab and 206 patients to placebo. DFS was improved compared with placebo in patients assigned to a regimen of every 3 weeks (Q3W; HR 0.44) and a regimen that includes dosing every 6 weeks (Q6W; HR 0.25). In the safety analysis set, 129 patients received Q3W only and 280 received Q3W start/Q6W switch. For cemiplimab-treated patients, observed sparse PK data and modelling indicate mean trough concentration at steady-state ($C_{trough,ss}$) was similar for both regimens. The model-predicted data indicates a modest reduction in mean $C_{trough,ss}$ (20.8%) and increase in mean maximum concentration at steady-state (51.3%) for Q3W start/Q6W switch regimen vs Q3W only (Table). Patients treated with Q3W start/Q6W switch had a lower incidence of grade ≥3 treatment-emergent adverse events (AEs), serious AEs, or AEs leading to treatment discontinuation compared with Q3W only.Table: 1660P

PK and safety of cemiplimab Q3W and Q3W start/Q6W switch regimens

	Cemiplimab 350 mg Q3W for 48 weeks	Cemiplimab 350 mg Q3W for 12 weeks/700 mg Q6W switch for 36 weeks
Pharmacokinetics, mean (SD)		
PK analysis set	n=59	n=112
Cycle 3 $C_{trough,ss}$,mg/L	56.5 (23.9)	49.0 (23.7)
MP $C_{trough,ss}$,mg/L	66.3 (30.7)	52.5 (31.4)
MP $C_{max,ss}$,mg/L	154 (43.1)	233 (64.9)
Safety, n (%)		
Safety analysis set	n=65	n=140
TEAEs, any grade	59 (90.8)	128 (91.4)

	Cemiplimab 350 mg Q3W for 48 weeks	Cemiplimab 350 mg Q3W for 12 weeks/700 mg Q6W switch for 36 weeks
TEAEs, grade 3–5	23 (35.4)	26 (18.6)
TE-SAEs	17 (26.2)	19 (13.6)
TEAEs leading to treatment discontinuation	16 (24.6)	4 (2.9)
TEAEs leading to death	1 (1.5)	1 (0.7)

$C_{max\ ss}$, maximum concentration at steady-state; MP, model-predicted; TEAE, treatment-emergent adverse event; TE-SAE, treatment-emergent serious adverse event.

Conclusions

Efficacy, PK and immunogenicity were similar between the Q3W and Q3W/Q6W switch regimens. The safety profile of cemiplimab regardless of dosing regimen was consistent with the known safety profile of cemiplimab in advanced solid malignancies. These results support cemiplimab 350 mg Q3W/700mg Q6W switch as a more convenient regimen for patients and health care providers.

Clinical trial identification

NCT03969004.

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