Supplementary material

Supplement 1. Study sites and principal investigators

Phase 2 Group 3 cemiplimab in patients with advanced cutaneous squamous cell carcinoma study sites and principal investigators

Site	Principal investigator	Patients recruited
Royal North Shore Hospital, St Leonards, New South Wales, Australia	Alexander Guminski	8
Peter Maccallum Cancer Centre, East Melbourne, Victoria, Australia	Danny Rischin	7
Sir Charles Gairdner Hospital, Nedlands, Western Australia, Australia	Annette Lim	7
H Lee Moffitt Cancer Center and Research Institute, Tampa, Florida, United States	Nikhil Khushalani	6
Dana Farber Cancer Institute, Boston, Massachusetts, United States	Chrysalyne Schmults	5
Washington University, St. Louis, Missouri, United States	Leonel Hernandez Aya	4
City of Hope, Duarte, California, United States	Badri Modi	3
Memorial Sloan Kettering Cancer Center, New York, United States	Lara Dunn	3
Royal Brisbane & Women's Hospital, Brisbane, Australia	Brett Hughes	2
Stanford Cancer Center, Redwood City, California, United States	Anne Lynn Chang	2
Universitätsklinikum Schleswig-Holstein, Kiel, Germany	Axel Hauschild	1
Medizinische Hochschule Hannover, Hannover, Germany	Ralf Gutzmer	1
Universitätsklinikum Essen, Essen, Germany	Dirk Schadendorf	1
Charitè Campus Mitte, Berlin, Germany	Claas Ulrich	1
Universitatsklinikum Tubingen, Tubingen, Germany	Thomas Eigentler	1

LMU Klinikum der Universität München, München, Germany	Carola Berking	1
University of Colorado, Aurora, Colorado, United States	Karl Lewis	1
University of California Los Angeles, Los Angeles, California, United States	Deborah Wong	1
Nebraska Methodist Hospital, Omah, Nebraska, United States	Yungpo Su	1
Northwestern University, Chicago, Illinois, United States	Sunandana Chandra	1
Huntsman Cancer Institute at The University of Utah, Salt Lake City, Utah, United States	Benjamin Voorhies	1
University of Rochester Medical Center, Rochester, New York, United States	Sherrif Ibrahim	1

5

6 **Phase 2 Group 1 cemiplimab in patients with advanced cutaneous squamous**

7 **cell carcinoma study sites and principal investigators**

Site	Principal investigator	Patients recruited
Peter Maccallum Cancer Centre, East Melbourne, Victoria, Australia	Danny Rischin	10
Royal Brisbane & Women's Hospital, Brisbane, Australia	Brett Hughes	4
Royal North Shore Hospital, St Leonards, New South Wales, Australia	Alexander Guminski	4
Universitätsklinikum Essen, Essen, Germany	Dirk Schadendorf	4
Dana Farber Cancer Institute, Boston, Massachusetts, United States	Chrysalyne Schmults	3
Sir Charles Gairdner Hospital, Nedlands, Western Australia, Australia	Annette Lim	2
Adelaide Cancer Centre, Kurralta Park, South Australia, Australia	Brian Stein	2
Universitätsklinikum Schleswig-Holstein, Kiel, Germany	Axel Hauschild	2
Charitè Campus Mitte, Berlin, Germany	Claas Ulrich	2
Universitatsklinikum Tubingen, Tübingen, Germany	Thomas Eigentler	2
MD Anderson Cancer Center, Houston, Texas, United States	Michael Migden	2
Memorial Sloan Kettering Cancer Center, New York, United States	Lara Dunn	2
Stanford Cancer Center, Redwood City, California, United States	Anne Lynn Chang	2
NYU Clinical Cancer Center, New York, United States	Anna Pavlick	2
Cleveland Clinic, Cleveland, Ohio, United States	Jessica Geiger	2
Universitätsklinikum Carl Gustav Carus an der TU Dresden, Dresden, Germany	Friedegund Meier	1
LMU Klinikum der Universität München, München, Germany	Carola Berking	1
City of Hope, Duarte, California, United States	Badri Modi	1

University of Colorado, Aurora, Colorado, United States	Karl Lewis	1
University of California Los Angeles, Los Angeles, California, United States	Deborah Wong	1
H Lee Moffitt Cancer Center and Research Institute, Tampa, Florida, United States	Nikhil Khushalani	1
Washington University, St. Louis, Missouri, United States	Leonel Hernandez Aya	1
Huntsman Cancer Institute at The University of Utah, Salt Lake City, Utah, United States	Benjamin Voorhies	1
Mount Sinai Comprehensive Cancer Center, Miami Beach, Florida, United States	Jose Lutzky	1
St. Luke's Hematology Oncology Specialists, Easton, Pennsylvania, United States	Sanjiv Agarwala	1
Massachusetts General Hospital, Boston, Massachusetts, United States	Chrysalyne Schmults	1

8

Supplement 2. Additional details on study methods

Details of tumor response assessments

Response assessments included radiologic scans (assessed per RECIST 1.1) for all patients, and digital medical photography (assessed per modified World Health Organization criteria) for patients with externally visible lesions. Composite response criteria were used for patients with both radiologic and photographic assessments. All radiologic response assessments were reviewed by a blinded ICR committee of radiologists. All digital medical photography assessments were reviewed by a blinded ICR committee of dermato-oncology experts. For patients with only radiologic assessments (no photography), only the assessments of the radiology ICR were required. For patients with both photographic and radiologic assessments, efficacy assessments were rendered by a multidisciplinary composite ICR committee that integrated the outputs of the radiology ICR committee and the photography ICR committee. For the Group 1 update, ICR committee members had discretion to revise assessments for previously reviewed timepoints if they felt it to be clinically appropriate upon review of additional imaging timepoints after the primary analysis.

Details of tumor biomarker procedures

Archived tumor samples from prior CSCC biopsies or surgeries were provided during the screening period. TMB was estimated in DNA samples extracted from formalin-fixed paraffin-embedded (FFPE) tumor biopsies. Genomic DNA was isolated from FFPE tissue using the QIAamp DNA FFPE Kit (Qiagen) and quantified using the Qubit® Fluorometer, following slide macrodissection to ensure >20% tumor content. Sequencing library was prepared using the TruSight Oncology 500® (TSO500) assay kit (Illumina). Briefly, tumor DNA (40ng/sample) was sheared using

a Covaris sonicator, followed by end base repair, A-tailing, adapter ligation and bead-based purification. Adapter-ligated samples were Polymerase Chain Reaction amplified to incorporate barcodes for sample multiplexing, followed by hybridization-based target region enrichment, library amplification and sequencing using the NovaSeq® platform. TMB was calculated as the total number of somatic single nucleotide variants and indels in the coding regions of targeted genes per megabase of analyzed genomic sequence. Germline and oncogenic driver gene variants were excluded from somatic mutations, according to the public database comparisons. In order to reduce the effect of FFPE DNA deamination artefacts on mutational variant calling, sequence reads from complementary DNA strands were identified using unique molecular identifier barcodes included in the assay protocol during the sequencing library generation.