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Initial results with IMA402 a PRAME-targeted T-cell receptor (TCR)-based bispecific T-cell engager (TCER) in advanced solid tumors

D. Schadendorf¹, J.C. Hassel², P. Harter³, R. Gutzmer⁴, M. Jalving⁵, L. Zimmer⁶, Y. Angela⁴, D. Heudobler⁷, F. Marmé⁸, B. Rack⁹, T. Schutte¹⁰, S. Spoerl¹¹, G. Stocker¹², G. Fiore¹³, K. Guenther¹⁴, S. Missel¹³, O. Veremchuk¹⁵, C.M. Britten¹⁶, C. Reinhardt¹⁶, M. Wermke¹⁷

¹ Dermatology Oncology, University Hospital Essen, Essen, Germany and German Cancer Consortium, Essen, Germany, ² Section of DermatoOncology, NCT - Nationales Zentrum für Tumorerkrankungen, Heidelberg, Germany, ³ Department of Gynaecology and Gynaecological Oncology, Ev. Kliniken Essen-Mitte, Essen, Germany, ⁴ Dermatology, Skin Cancer Center, Johannes Weseling Klinikum, Minden, Germany, ⁵ Medical Oncology, UMCG - University Medical Center Groningen, Groningen, Netherlands, ⁶ Dermatology, University Hospital Essen, Essen, Germany, ⁷ Department of Internal Medicine III, UKR - University Hospital Regensburg, Regensburg, Germany, ⁸ Department of Obstetrics and Gynecology, Medical Faculty Mannheim of the Heidelberg University, University Medical Centre Mannheim, Mannheim, Germany, ⁹ Department of Gynecology and Obstetrics, Ulm University Hospital, Ulm, Germany, ¹⁰ Department of Medical Oncology, The Netherlands Cancer Institute (NKI), Amsterdam, Netherlands, ¹¹ Department of Internal Medicine-Haematology and Oncology, Uniklinikum Erlangen, Friedrich-Alexander University Erlangen-Nürnberg (FAU), Erlangen, Germany, ¹² University Cancer Center Leipzig UCCL, Department of Medicine (Oncology, Gastroenterology, Hepatology and Pulmonology) and University Cancer Center Leipzig, Cancer Center Central Germany (CCCG), Leipzig, Germany, ¹³ Translational Science Department, Immatics Biotechnologies GmbH, Munich, Germany, ¹⁴ Department of Translational Science Department, Immatics Biotechnologies GmbH, Tuebingen, Germany, ¹⁵ Oncology Dept., Immatics Biotechnologies GmbH, Munich, Germany, ¹⁶ CMO, Immatics Biotechnologies N.V., Munich, Germany ¹⁷ NCT/UCC Early Clinical Trial Unit, TU Dresden University of Technology, Dresden, Germany

Background

IMA402 is a next-generation TCR-based bispecific (TCER) designed to redirect T cells to PRAME+ tumor cells. It combines a high-affinity, highly specific TCR domain against an HLA-A*02:01-presented PRAME-derived peptide with a low-affinity T-cell–recruiting domain for improved tolerability and biodistribution, and an Fc part for half-life extension. IMA402-101 (NCT05958121) is a first-in-human Ph 1/2 basket study evaluating IMA402 in advanced solid tumors.

Methods

Pts were ≥18 y, HLA-A*02:01+, had R/R solid tumors, measurable disease (RECIST 1.1), ECOG PS 0-1, and had exhausted available treatment options. Dose escalation used an adaptive design (BLRM) with cohorts of 1-6 pts. Doses ranged from 0.02-30 mg IMA402, with up to 3 step doses. Primary endpoints were safety and MTD/TP2D. Secondary endpoints included antitumor activity measures.

Results

As of Sep 26, 2025, 80 heavily pretreated pts (median 3 prior lines; range 1-7) received IMA402 at escalating doses. The most frequent TRAEs were low-grade CRS at initial doses (G1: 33%; G2: 5%; ≥G3: 1%), transient lymphopenia (all G: 50%; ≥G3: 38%), and arthralgia (all G: 26%; ≥G3: 1%). No ICANS or IMA402-related G5 events occurred. The MTD was not reached at 30 mg; TP2D range was determined as ≥10 mg. Of 57 efficacy-evaluable pts, 20 were treated at the TP2D range. The confirmed ORR (cORR) at the TP2D range across all indications was 30% (6/20; all responses ongoing at data cutoff); disease control rate (DCR) was 65% (13/20). Clinical activity was noted in melanoma (cORR: 29% [4/14]; DCR: 71% [10/14]), including 2 complete metabolic responses in cutaneous and uveal melanoma ongoing at 8 and 18 mo, respectively, and ovarian carcinoma (OC) with 2/3 confirmed responses, including 1 ongoing confirmed PR with 100% reduction in target lesions. Melanoma and OC responses occurred in pts who were ICI and platinum resistant, respectively.

Conclusions

IMA402 demonstrated favorable tolerability and encouraging antitumor activity in heavily pretreated pts with advanced solid tumors, notably melanoma and OC, at the TP2D range. Ph1b/2 cohorts are planned to further evaluate IMA402 targeting PRAME, including potentially synergistic combination regimens and earlier lines of therapy.

Clinical trial identification

NCT05958121.

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Legal entity responsible for the study

Immatics Biotechnologies GmbH.

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Disclosure

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Hassel: Financial Interests, Personal, Invited Speaker: BMS, Novartis, MSD, Sunpharma, Pierre Fabre, Immunocore, Delcath, Amgen, Replimune, Regeneron; Financial Interests, Institutional, Advisory Board: MSD, Pierre Fabre, Novartis, BMS, Immunocore, Philogen; Financial Interests, Personal, Advisory Board: Sunpharma, Onkowissen; Financial Interests, Institutional, Local PI: Philogen, Genentech, BioNTech, Iovance, Pierre Fabre, Regeneron, Sanofi, Replimune, Immatics, MSD, Pfizer; Financial Interests, Institutional, Coordinating PI: BMS, Immunocore, Novartis, Genmab; Financial Interests, Personal, Steering Committee Member: Immunocore, IO Biotech; Non-Financial Interests, Leadership Role: DeCOG; Non-Financial Interests, Member: ASCO. P. Harter: Financial Interests, Personal, Advisory Board, Value includes honoraria for lectures: AstraZeneca; Financial Interests, Personal, Advisory Board, includes honoraria for lectures: GSK, Roche, MSD; Financial Interests, Personal, Invited Speaker: Amgen, Stryker, Zailab, Eisai, Daiichi Sankyo; Financial Interests, Personal, Advisory Board: Clovis, Immunogen, Novartis, Mersana, Miltenyi, Exscientia, Corcept, BionTech, Karyopharm, AbbVie, Zymeworks, Lilly, BeOne, Gilead, Immunocore; Financial Interests, Personal, Other, IDMC member: Sotio; Financial Interests, Institutional, Trial Chair: AstraZeneca, Roche, GSK, Immunogen, MSD; Financial Interests, Institutional, Local PI: AbbVie, AbbVie, Immatics, Genmab; Financial Interests, Institutional, Funding: Seagen, Clovis; Financial Interests, Institutional, Other, Co-investigator: Novartis; Non-Financial Interests, Principal Investigator: AstraZeneca; Other, Travel support for conference: AstraZeneca, AbbVie. R. Gutzmer: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, Pierre Fabre, Novartis, Merck Sharp Dohme, Merck Serono, Almirall, Immunocore, Delcath, Kyowa Kirin, Sanofi, SUN Pharma, Regeneron, Incyte; Financial Interests, Personal, Invited Speaker: Bristol Myers Squibb, Pierre Fabre, Novartis, Merck Sharp Dohme, Merck Serono, Almirall, Sanofi, SUN Pharma, Regeneron, Incyte; Financial Interests, Institutional, Research Grant: Kyowa Kirin, Almirall, SUN Pharma, Amgen, Sanofi/Regeneron, Merck Serono, Recordati; Non-Financial Interests, Member of Board of Directors: DeCOG; Other, Travel and meeting support: Pierre Fabre, SUN Pharma, Almirall. M. Jalving: Financial Interests, Institutional, Advisory Board, Advisory Board: AstraZeneca; Financial Interests, Institutional, Advisory Board, Advisory board: Merck; Financial Interests, Institutional, Advisory Board: Pierre Fabre, Regeneron. L. Zimmer: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, Novartis, MSD, Pierre Fabre, Regeneron; Financial Interests, Personal, Invited Speaker: Novartis, MSD, Sunpharma, Pierre Fabre, Regeneron; Financial Interests, Personal, Other, Travel Support: Sunpharma, Pierre Fabre, Novartis; Financial Interests, Institutional, Research Grant: Novartis; Non-Financial Interests, Member: German Cancer Society, Dermatologic Cooperative Oncology Group, European Association of Dermato-Oncology. D. Heudobler: Financial Interests, Personal, Advisory Board: Boehringer Ingelheim, Bristol Myers Squibb, Janssen-Cilag, MSD, Bristol Myers Squibb, GSK, Immatics; Financial Interests, Personal, Invited Speaker: Bristol Myers Squibb, MSD, Roche, AbbVie; Financial Interests, Personal, Other, Travel, Accommodations, Expenses: Sanofi, AbbVie, Janssen-Cilag; Financial Interests, Personal, Other, Travel, Accommodation, Expenses: BeOne Medicines; Financial Interests, Institutional, Funding: Janssen-Cilag, Bristol Myers Squibb. F. Marmé: Financial Interests, Personal, Invited Speaker: AstraZeneca, GSK, Pfizer, Lilly, Daiichi Sankyo; Financial Interests, Personal, Advisory Board: AstraZeneca, MSD, Novartis, Roche, Gilead Sciences, Eisai, GenomicHealth, Myriad, Seagen, Daiichi Sankyo, Biontech, Incyte, Novocure, Nerviano; Financial Interests, Institutional, Invited Speaker: Seagen, Daiichi Sankyo, GSK, AstraZeneca, Stemline Menarini; Financial Interests, Institutional, Advisory Board: Roche, Immunicom; Financial Interests, Institutional, Local PI: Roche, Novartis, Eisai, MSD, Vaccibody, GSK, Daiichi Sankyo, Böhringer Ingelheim; Financial Interests, Institutional, Coordinating PI: AstraZeneca, Roche, Gilead Sciences, German Breast Group, AGO Research GmbH, Menarini-Stemline; Financial Interests, Institutional, Funding: AstraZeneca, Lilly, Seagen. G. Stocker: Financial Interests, Personal, Advisory Board, Discussion latest results on upper GI Cancer: BMS; Financial Interests, Personal, Other, virtual Access to ASCO GI 2025: AstraZeneca; Financial Interests, Personal, Other, travel compensation ESMO GI 2024: Gilead; Non-Financial Interests, Member, regular Member: Deutsche Gesellschaft für Hamatologie und Onkologie, Arbeitsgemeinschaft für Internistische Onkologie (AIO), Deutsche Gesellschaft für Innere Medizin. G. Fiore: Financial Interests, Personal, Full or part-time Employment: Immatics. K. Guenther: Financial Interests, Full or part-time Employment: Immatics. S. Missel: Financial Interests, Personal, Full or part-time Employment: Immatics. O. Veremchuk: Financial Interests, Personal, Full or part-time Employment: Immatics. C.M. Britten: Financial Interests, Personal, Full or part-time Employment: Immatics; Financial Interests, Officer: Immatics. C. Reinhardt: Financial Interests,

Personal, Full or part-time Employment: Immatics; Financial Interests, Personal, Officer: Immatics. M. Wermke: Financial Interests, Personal, Speaker, Consultant, Advisor: Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, BMS, Daiichi Sankyo Europe GmbH, Genetech, ImCheck, Immatics, Iovance, Lilly, t-Knife, Roche; Financial Interests, Institutional, Funding: Roche, Iovance, Boehringer Ingelheim. All other authors have declared no conflicts of interest.

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