9-1-2021

961MO Safety, efficacy, immunogenicity of arenavirus-based vectors HB-201 and HB-202 in patients with HPV16+ cancers

M R. Posner

A L. Ho

J Niu

L Nabell

R S. Leidner

See next page for additional authors

Authors

M R. Posner, A L. Ho, J Niu, L Nabell, R S. Leidner, J Nieva, D L. Richardson, A T. Pearson, Ding Wang, K Chung, D R. Adkins, A Pimentel, S Wong, C Lacobucci, X Qing, K Katchar, K Schlienger, I Matushansky, S Fu, and D G. Pfister

Personal, Advisory Board: Astellas; Financial Interests, Personal, Advisory Board: Otsuka; Financial Interests, Institutional, Research Grant: Abbvie; Financial Interests, Institutional, Research Grant: Acerta Pharma; Financial Interests, Institutional, Research Grant: Adaptimmune; Financial Interests, Institutional, Research Grant: Amgen; Financial Interests, Institutional, Research Grant: Apexigen; Financial Interests, Institutional, Research Grant: Arcus; Financial Interests, Institutional, Research Grant: Array; Financial Interests, Institutional, Research Grant: AstraZeneca; Financial Interests, Institutional, Research Grant: Atreca; Financial Interests, Institutional, Research Grant: BeiGene; Financial Interests, Institutional, Research Grant: Birdie; Financial Interests, Institutional, Research Grant: Boehringer Ingelheim; Financial Interests, Institutional, Research Grant: Checkpoint Therapeutics; Financial Interests, Institutional, Research Grant: Corvus; Financial Interests, Institutional, Research Grant: CytomX; Financial Interests, Institutional, Research Grant: Daiichi Sankyo; Financial Interests, Institutional, Research Grant: Dynavax; Financial Interests, Institutional, Research Grant: EMD Serono; Financial Interests, Institutional, Research Grant: Genentech/Roche; Financial Interests, Institutional, Research Grant: Genocea; Financial Interests, Institutional, Research Grant: GlaxoSmithKline; Financial Interests, Institutional, Research Grant: Gritstone Oncology; Financial Interests, Institutional, Research Grant: Guardant; Financial Interests, Institutional, Research Grant: Hengrui; Financial Interests, Institutional, Research Grant: Immunocore; Financial Interests, Institutional, Research Grant: Incyte; Financial Interests, Institutional, Research Grant: Janssen; Financial Interests, Institutional, Research Grant: Jounce; Financial Interests, Institutional, Research Grant: Kadmon; Financial Interests, Institutional, Research Grant: Lilly; Financial Interests, Institutional, Research Grant: Loxo; Financial Interests, Institutional, Research Grant: Lycera; Financial Interests, Institutional, Research Grant: Merck; Financial Interests, Institutional, Research Grant: Mirati; Financial Interests, Institutional, Research Grant: Neovia; Financial Interests, Institutional, Research Grant: Novartis; Financial Interests, Institutional, Research Grant: OncoMed; Financial Interests, Institutional, Research Grant: Pfizer; Financial Interests, Institutional, Research Grant: Regeneron; Financial Interests, Institutional, Research Grant: Ribon; Financial Interests, Institutional, Research Grant: Sanofi; Financial Interests, Institutional, Research Grant: Shattuck Labs; Financial Interests, Institutional, Research Grant: Stem CentRx; Financial Interests, Institutional, Research Grant: Syndax; Financial Interests, Institutional, Research Grant: Takeda; Financial Interests, Institutional, Research Grant: Tarveda Therapeutics; Financial Interests, Institutional, Research Grant: TCR2 Therapeutics; Financial Interests, Institutional, Research Grant: University of Michigan; Financial Interests, Institutional, Research Grant: WindMIL. D. Carbone: Financial Interests, Institutional, Research Grant: Gritstone bio, Inc.; Financial Interests, Personal, Research Grant: Bristol-Myers Squibb; Financial Interests, Personal, Advisory Board: Abbvie; Financial Interests, Personal, Advisory Board: Bayer; Financial Interests, Personal, Advisory Board: AstraZeneca; Financial Interests, Personal, Advisory Board: Biocept; Financial Interests, Personal, Advisory Board: Boehringer Ingelheim; Financial Interests, Personal, Advisory Board: Clovis; Financial Interests, Personal, Advisory Board: EMD Serono; Financial Interests, Personal, Advisory Board: Foundation Medicine; Financial Interests, Personal, Advisory Board: Genentech/Roche; Financial Interests, Personal, Advisory Board: GlaxoSmithKline; Financial Interests, Personal, Advisory Board: Guardant Health; Financial Interests, Personal, Advisory Board: Helsinn; Financial Interests, Personal, Advisory Board: Incyte; Financial Interests, Personal, Advisory Board: Inivata; Financial Interests, Personal, Advisory Board: Inovio; Financial Interests, Personal, Advisory Board: Janssen; Financial Interests, Personal, Advisory Board: Merck; Financial Interests, Personal, Advisory Board: MSD; Financial Interests, Personal, Advisory Board: Novartis Oncology; Financial Interests, Personal, Advisory Board: Peregrine Pharmaceuticals; Financial Interests, Personal, Advisory Board: Pfizer; Financial Interests, Personal, Advisory Board: Synta; Financial Interests, Personal, Advisory Board: Loxo; Financial Interests, Personal, Research Grant: Bristol-Myers Squibb; Financial Interests, Personal, Advisory Board: Nexus. B. Johnson: Financial Interests, Personal, Advisory Board: Gritstone bio, Inc.; Financial Interests, Personal, Advisory Board: Incyte; Financial Interests, Personal, Advisory Board: Taiho Oncology; Financial Interests, Personal, Research Grant: Bristol-Myers Squibb; Financial Interests, Personal, Research Grant: Syntrix. S. Roychowdhury: Financial Interests, Institutional, Stocks/Shares: Johnson&Johnson; Financial Interests, Personal, Advisory Board: Abbvie; Financial Interests, Personal, Advisory Board: Incyte; Financial Interests, Personal, Advisory Board: Merck; Financial Interests, Personal, Advisory Board: QED Therapeutics; Financial Interests, Personal, Research Grant: Ignyta; Financial Interests, Personal, Research Grant: Incyte; Financial Interests, Personal, Research Grant: QED Therapeutics; Financial Interests, Personal, Research Grant: Takeda. K. Mody: Financial Interests, Personal, Advisory Board: AstraZeneca; Financial Interests, Personal, Advisory Board: Celgene; Financial Interests, Personal, Advisory Board: Eisai; Financial Interests, Personal, Advisory Board: Genentech/Roche; Financial Interests, Personal, Advisory Board: Merrimack; Financial Interests, Personal, Advisory Board: Vicus Therapeutics; Financial Interests, Personal, Research Grant: Agios; Financial Interests, Personal, Research Grant: Ariad; Financial Interests, Personal, Research Grant: ArQule; Financial Interests, Personal, Research Grant: FibroGen; Financial Interests, Personal, Research Grant: MedImmune; Financial Interests, Personal, Research Grant: Senhwa Biosciences; Financial Interests, Personal, Research Grant: Taiho Pharmaceutical; Financial Interests, Personal, Research Grant: TRACON Pharma; Financial Interests, Personal, Advisory Board: Ipsen; Financial Interests, Institutional, Research Grant: AstraZeneca; Financial Interests, Institutional, Research Grant: Gritstone Oncology; Financial Interests, Institutional, Research Grant: Incyte; Financial Interests, Institutional, Research Grant: Merck; Financial Interests, Institutional, Research Grant: Basilea; Financial Interests, Personal, Stocks/Shares: CytoDyn; Financial Interests, Personal, Stocks/Shares: Oncotherapeutics. E. Bournazou: Financial Interests, Personal, Full or part-time Employment: Bristol Myers Squibb. D. Schenk: Financial Interests, Personal, Full or part-time Employment: Gritstone bio, Inc. S. Kounlavouth: Financial Interests, Personal, Full or part-time Employment: Gritstone bio, Inc. L. Kraemer: Financial Interests, Personal, Full or part-time Employment: Gritstone bio, Inc. G. Talbot: Financial Interests, Personal, Full or part-time Employment: Gritstone bio, Inc. R. Rousseau: Financial Interests, Personal, Full or part-time Employment: Gritstone bio, Inc.; Financial Interests, Personal, Stocks/Shares: Gritstone bio, Inc. A.R. Ferguson: Financial Interests, Personal, Full or part-time Employment: Gritstone bio, Inc.; Financial Interests, Personal, Stocks/Shares: Gritstone bio, Inc. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2021.08.1345

961MO Safety, efficacy, immunogenicity of arenavirus-based vectors HB-201 and HB-202 in patients with HPV16+ cancers

M.R. Posner[1], A.L. Ho[2], J. Niu[3], L. Nabell[4], R.S. Leidner[5], J. Nieva[6], D.L. Richardson[7], A.T. Pearson[8], D. Wang[9], K. Chung[10], D.R. Adkins[11], A. Pimentel[12], S. Wong[13], C. Lacobucci[14], X. Qing[15], K. Katchar[16], K. Schlienger[17], I. Matushansky[18], S. Fu[19], D.G. Pfister[20]

[1]Hematology and Medical Oncology, Icahn School of Medicine at Mount Sinai, New York, NY, USA; [2]Medical Oncology; Department of Medicine, Memorial Sloan Kettering Cancer Center; Weill Cornell Medical College, New York, NY, USA; [3]TW Lewis Melanoma Center of Excellence, Banner MD Anderson Cancer Center, Gilbert, AZ, USA; [4]O'Neal Comprehensive Cancer Center, University of Alabama Hospital, Birmingham, AL, USA; [5]Earle A. Chiles Research Institute, Providence Cancer Institute, Portland, OR, USA; [6]Clinical Medicine, University of Southern California, Los Angeles, CA, USA; [7]Gynecologic Oncology Department, Stephenson Cancer Center/University of Oklahoma/Sarah Cannon Research Institute, Oklahoma City, OK, USA; [8]Hematology and Oncology, University of Chicago Medical Center, Chicago, IL, USA; [9]Medical Oncology, Henry Ford Hospital, Detroit, MI, USA; [10]Cancer Institute, Greenville Hospital System University Medical Center (ITOR), Greenville, SC, USA; [11]Division of Oncology, Washington University School of Medicine in St. Louis, St. Louis, MO, USA; [12]Sylvester Comprehensive Caner Center, University of Miami, Miami, FL, USA; [13]Cancer Center - Froedtert Hospital, Medical College of Wisconsin, Milwaukee, WI, USA; [14]Clinical Programs and Operations Logistics, Hookipa Pharma Inc., New York, NY, USA; [15]Clinical Science, Hookipa Pharma Inc., New York, NY, USA; [16]Translational and Clinical Biomarkers, Hookipa Pharma Inc., New York, NY, USA; [17]Immuno-Oncology, Hookipa Pharma Inc., New York, NY, USA; [18]Research and Development, Hookipa Pharma Inc., New York, NY, USA; [19]Investigational Cancer Therapeutics, University of Texas M.D. Anderson Cancer Center, Houston, TX, USA; [20]Head and Neck Oncology Service, Memorial Sloan Kettering Cancer Center, New York, NY, USA

Background: Human papillomavirus 16 positive (HPV16+) cancers are caused by stable expression of HPV16-specific E7 and E6 oncoproteins, also a source of immunogenic neoantigens. Replicating arenavirus vectors HB-201 (LCMV) and HB-202 (Pichinde virus), expressing the same non-oncogenic HPV16 E7E6 fusion protein, induce tumour-specific T-cell responses.

Methods: A phase I first-in-human study assessed HB-201 monotherapy and HB-201 & HB-202 alternating 2-vector therapy (HB-201/HB-202) intravenously (IV) with or without 1 intratumoral dose (IT/IV) in HPV16+ cancers. Safety, tolerability, and preliminary anti-tumour activity by Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 or immune RECIST were evaluated, as well as immunogenicity and pharmacodynamic biomarkers in blood and tumour tissue samples.

Results: The study treated 38 patients (29 with $\geq$1 efficacy scan) with confirmed HPV16+ cancers with a median (range) of 3 (1—10) prior anticancer therapies. The most common primary cancer site was oropharynx (76%), followed by cervical (7.9%). Eighteen patients received HB-201 monotherapy IV and 9 IT/IV; 11 patients received HB-201/HB-202 alternating therapy. Treatment was generally well tolerated. Twenty patients (53%) reported treatment-related adverse events (all Grade $\leq$2). Two of 11 evaluable patients treated with HB-201 IV every 3 weeks had partial response (including 1 unconfirmed immune complete response of target lesion) and 6 had stable disease (SD) lasting 1.2—5.9 months. All 6 evaluable patients that received HB-201/HB-202 had SD. HPV16-specific T-cells in peripheral blood were detected at several time points post-administration through direct *ex vivo* stimulation. Different schedules, regimens, modes of administration, and doses will be presented with corresponding immunogenicity data. The proposed pathway to the recommended phase II regimen will be discussed.

Conclusions: Arenavirus-based vectors HB-201 and HB-201/HB-202 appeared well tolerated and showed preliminary anti-tumour activity as single agents in this heavily pretreated population of patients with HPV16+ cancers. Induction of circulating E7E6-specific activated CD8+ T-cells was observed.

Clinical trial identification: NCT04180215.

Editorial acknowledgement: Writing and editorial support was provided by Margaret Van Horn, PhD, of AlphaBioCom, LLC, and was funded by Hookipa Biotech GmbH.

Legal entity responsible for the study: Hookipa Biotech GmbH.

Funding: Hookipa Biotech GmbH.

Disclosure: M.R. Posner: Other, Principal Investigator: Hookipa Pharma; Financial Interests, Advisory Role: BioNTech; Financial Interests, Advisory Role: Kura; Financial Interests, Advisory Board: Cel-Sci; Financial Interests, Advisory Board: Merck; Financial Interests, Advisory Role: Hookipa; Financial Interests; Advisory Role: Naveris; Financial Interests, Institutional, Funding: Formation Biologics; Financial Interests, Institutional, Funding: Innate; Financial Interests, Institutional, Funding: Hookipa Pharma; Financial Interests, Institutional, Funding: Sensei; Financial Interests, Institutional, Funding: Regeneron (Clinical Trials); Financial Interests, Royalties: Alopexx; Financial Interests, Institutional, Royalties: anti-Pseudomonas antibody; Financial Interests, Institutional, Royalties: anti-Staphylococcal monoclonal antibody; Financial Interests, Royalties: UpToDate editor; Financial Interests, Advisory Board: Hookipa Pharma. A.L. Ho: Other, Principal Investigator: Hookipa Pharma; Financial Interests, Institutional, Other, Honoraria: Massachusetts General Hospital; Financial Interests, Institutional, Other, Honoraria: Winship Cancer Center/Emory; Financial Interests, Institutional, Other, Honoraria: Leidos/NIH; Financial Interests, Institutional, Other, Honoraria: ASTRO; Financial Interests, Institutional, Other, Honoraria: Rasopathy conference; Financial Interests, Advisory Role: Eisai; Financial Interests, Advisory Role: Sanofi Genzyme; Financial Interests, Advisory Role: Ayala Pharmaceuticals; Financial Interests, Advisory Role: Regeneron; Financial Interests, Advisory Role: CureVac; Financial Interests, Advisory Role: Klus Pharm; Financial Interests, Advisory Role: Prelude Therapeutics; Financial Interests, Advisory Role: Novartis; Financial Interests, Advisory Role: Kura Oncology; Financial Interests, Advisory Role: AstraZeneca; Financial Interests, Advisory Role: Merck; Financial Interests, Advisory Role: Bristol-Myers Squibb; Financial Interests, Advisory

Role: Genentech/Roche; Financial Interests, Advisory Role: Sun Pharmaceuticals; Financial Interests, Advisory Role: TRM Oncology; Financial Interests, Advisory Role: McGivney Global Advisors; Financial Interests, Advisory Role: Rgenta; Financial Interests, Advisory Role: Exelixis; Financial Interests, Advisory Role: Affyimmune; Financial Interests, Advisory Role: Inxmed; Financial Interests, Speaker's Bureau: Medscape; Financial Interests, Speaker's Bureau: Novartis; Financial Interests, Speaker's Bureau: Omniprex America; Financial Interests, Personal, Funding, For Clinical Trials: Allos Therapeutics; Financial Interests, Personal, Funding, For Clinical Trials: Astellas Pharma; Financial Interests, Personal, Funding, For Clinical Trials: AstraZeneca; Financial Interests, Personal, Funding, For Clinical Trials: Ayala Pharmaceuticals; Financial Interests, Personal, Funding, For Clinical Trials: Bayer; Financial Interests, Personal, Funding, For Clinical Trials: Bristol-Myers Squibb; Financial Interests, Personal, Funding, For Clinical Trials: Daiichi Sankyo; Financial Interests, Personal, Funding, For Clinical Trials: Eisai; Financial Interests, Personal, Funding, For Clinical Trials: Elevar Therapeutics; Financial Interests, Personal, Funding, For Clinical Trials: Genentech/Roche; Financial Interests, Personal, Funding, For Clinical Trials: Celldex; Financial Interests, Personal, Funding, For Clinical Trials: Kura Oncology; Financial Interests, Personal, Funding, For Clinical Trials: Lilly; Financial Interests, Personal, Funding, For Clinical Trials: Merck; Financial Interests, Personal, Funding, For Clinical Trials: Novartis; Financial Interests, Personal, Funding, For Clinical Trials: Pfizer; Financial Interests, Personal, Funding, For Clinical Trials: Kura Oncology; Financial Interests, Other, Travel/Accommodation/Expenses: Ayala Pharmaceuticals; Financial Interests, Other, Travel/Accommodation/Expenses: Ignyta; Financial Interests, Other, Travel/Accommodation/Expenses: Janssen Oncology; Financial Interests, Other, Travel/Accommodation/Expenses: Klus Pharma; Financial Interests, Other, Travel/Accommodation/Expenses: Kura Oncology; Financial Interests, Other, Travel/Accommodation/Expenses: Merck; Financial Interests, Other, Travel/Accommodation/Expenses: Shanghai Jia Tong University; Financial Interests, Stocks/Shares: Rgenta; Financial Interests, Member of the Board of Directors: International Thyroid Oncology Group. J. Niu: Other, Principal Investigator: Hookipa Pharma; Financial Interests, Advisory Role: Boehringer Ingelheim; Financial Interests, Advisory Role: Merck; Financial Interests, Advisory Role: AstraZeneca; Financial Interests, Advisory Role: Blueprint Medicines; Financial Interests, Advisory Role: Immvira; Financial Interests, Advisory Role: Johnson&Johnson; Financial Interests, Advisory Role: Takeda; Financial Interests, Advisory Role: Exelixis; Financial Interests, Advisory Role: Beigene; Financial Interests, Advisory Role: Mirati Therapeutics. L. Nabell: Other, Principal Investigator, NCT04180215: Hookipa Pharma. R.S. Leidner: Other, Principal Investigator, NCT04180215: Hookipa Pharma; Financial Interests, Advisory Role: Sanofi/Regeneron; Financial Interests, Advisory Role: AstraZeneca; Financial Interests, Advisory Role: Merck; Financial Interests, Advisory Role: Bristol-Myers Squibb; Financial Interests, Advisory Role: Oncolys Biopharma; Financial Interests, Institutional, Funding: Bristol-Myers Squibb; Financial Interests, Institutional, Funding: MedImmune; Financial Interests, Other, Travel/Accommodation/Expenses: Sanofi/Regeneron; Financial Interests, Other, Travel/Accommodation/Expenses: AstraZeneca; Financial Interests, Other, Travel/Accommodation/Expenses: Merck; Financial Interests, Other, Travel/Accommodation/Expenses: Bristol-Myers Squibb. J. Nieva: Other, Principal Investigator: Hookipa Pharma; Financial Interests, Advisory Role: AstraZeneca; Financial Interests, Advisory Role: Bayer; Financial Interests, Advisory Role: Western Oncolytics; Financial Interests, Advisory Role: Fujirebio Diagnostics; Financial Interests, Advisory Role: Takeda; Financial Interests, Advisory Role: Roche/Genentech; Financial Interests, Advisory Role: Turnstone; Financial Interests, Institutional, Funding: Merck; Financial Interests, Institutional, Funding: Genentech; Financial Interests, Stocks/Shares: Epic Sciences; Financial Interests, Stocks/Shares: Cansera; Financial Interests, Royalties: Patent Pending - movement and unexpected health care encounters. D.L. Richardson: Other, Principal Investigator: Hookipa Pharma; Financial Interests, Advisory Role: AstraZeneca; Financial Interests, Advisory Role: Genentech/Roche; Financial Interests, Advisory Role: Deciphera; Financial Interests, Advisory Role: Mersana; Financial Interests, Advisory Role: Tesaro/GlaxoSmithKline; Financial Interests, Institutional, Funding: AstraZeneca; Financial Interests, Institutional, Funding: Genentech/Roche; Financial Interests, Institutional, Funding: Mersana; Financial Interests, Institutional, Funding: Tesaro/GlaxoSmithKline; Financial Interests, Institutional, Funding: Aravive; Financial Interests, Institutional, Funding: ArQule, Inc.; Financial Interests, Institutional, Funding: Decphera; Financial Interests, Institutional, Funding: Harpoon Therapeutics; Financial Interests, Institutional, Funding: Innovent Biologics; Financial Interests, Institutional, Funding: Karyopharm; Financial Interests, Institutional, Funding: Merck; Financial Interests, Institutional, Funding: Syros Pharmaceuticals; Financial Interests, Institutional, Funding: Five Prime Therapeutics; Financial Interests, Institutional, Funding: Hookipa Biotech; Financial Interests, Institutional, Funding: FujiFilm; Financial Interests, Institutional, Funding: Shattuck Labs; Financial Interests, Institutional, Funding: Plexxikon. A.T. Pearson: Other, Principal Investigator: Hookipa Pharma; Financial Interests, Advisory Role: Prelude Therapeutics; Financial Interests, Expert Testimony: Smith Haughey Rice & Roegge. D. Wang: Other, Principal Investigator: Hookipa Pharma; Financial Interests, Advisory Role: Castle BioSciences; Financial Interests, Advisory Role: Qurgen; Financial Interests, Other, Travel/Accommodation/Expenses: Castle BioSciences; Financial Interests, Other, Travel/Accommodation/Expenses: Qurgen. K. Chung: Other, Principal Investigator: Hookipa Pharma. D.R. Adkins: Other, Principal Investigator: Hookipa Pharma; Financial Interests, Advisory Role: Merck; Financial Interests, Advisory Role: Cue Biopharma; Financial Interests, Advisory Role: BLU; Financial Interests, Advisory Role: Exelixis; Financial Interests, Advisory Role: Kura; Financial Interests, Advisory Role: Twoxar; Financial Interests, Advisory Role: Vaccinex; Financial Interests, Advisory Role: Zilio; Financial Interests, Advisory Role: Targimmune; Financial Interests, Institutional, Funding: Pfizer; Financial Interests, Institutional, Funding: Eli Lilly; Financial Interests, Institutional, Funding: Merck; Financial Interests, Institutional, Funding: Celgene/BMS; Financial Interests, Institutional, Funding: Novartis; Financial Interests, Institutional, Funding: AstraZeneca; Financial Interests, Institutional, Funding: Atara Bio; Financial Interests, Institutional, Funding: Blueprint Medicine; Financial Interests, Institutional, Funding: Celldex; Financial Interests, Institutional, Funding: Aduro; Financial Interests, Institutional, Funding: Enzychem; Financial Interests, Institutional, Funding: Kura; Financial Interests, Institutional, Funding: Exelixis; Financial Interests, Institutional, Funding: Innate; Financial Interests, Institutional, Funding: Sensei; Financial Interests, Institutional, Funding: Matrix Biomed; Financial Interests, Institutional, Funding: ISA; Financial Interests, Institutional, Funding: Cofactor; Financial Interests, Institutional, Funding: Cue Biopharma; Financial Interests, Institutional, Funding: Debiopharm; Financial Interests, Institutional, Funding: Epizyme; Financial Interests, Institutional, Funding: Hookipa; Financial Interests, Institutional, Funding: Shanghai De Novo; Financial Interests, Institutional, Funding: Roche. A. Pimentel: Other, Principal Investigator: Hookipa Pharma; Other, Principal Investigator: Turnstone Biologics, Corp; Other, Principal Investigator: Ludwig Institute for Cancer Research, Ltd; Other, Principal Investigator: Isofol Medical AB; Other, Principal Investigator: Hoosier Cancer Research Network, Inc.; Other, Principal Investigator: ECOG-ACRIN; Financial Interests, Advisory Role: Taiho Oncology; Financial Interests, Advisory Role: QED Therapeutics; Financial Interests, Advisory Role: Bristol-Myers Squibb Company; Financial Interests, Stocks/Shares: Pfizer; Financial Interests, Stocks/Shares: BioNTech. S. Wong: Other, Principal Investigator: Hookipa Pharma. C. Iacobucci: Financial Interests, Stocks/Shares: BMS; Financial Interests, Stocks/Shares: Hookipa Pharma; Financial Interests, Full or part-time Employment: Hookipa Pharma. X. Qing: Financial Interests, Stocks/Shares: Hookipa Pharma; Financial Interests, Full or part-time Employment: Hookipa Pharma. K. Katchar: Financial Interests, Stocks/Shares: Hookipa Pharma; Financial Interests, Full or part-time Employment: Hookipa Pharma. K. Schlienger: Financial Interests, Other, Travel/Accommodation/Expenses: Hookipa Pharma; Financial Interests, Full or part-time Employment: Hookipa Pharma. I. Matushansky: Financial Interests, Stocks/Shares: Hookipa Pharma; Financial Interests, Full or part-time Employment: Hookipa Pharma; Financial Interests, Member of the Board of Directors: Crescendo Biologics; Financial Interests, Leadership Role: Hookipa Pharma. S. Fu: Other, Principal Investigator: Hookipa Pharma; Financial Interests, Personal, Funding: Millenium Pharmaceuticals, Inc.; Financial Interests, Personal, Funding: Sorcimed Biopharma, Inc.; Financial Interests, Personal, Funding: Exelixis; Financial Interests, Personal, Funding: BeiGene; Financial Interests, Personal, Funding: Novocure; Financial Interests, Institutional, Funding: AstraZeneca; Financial Interests, Institutional, Funding: Abbisko; Financial Interests, Institutional, Funding: Anaeropharma Science; Financial Interests, Institutional, Funding: Arrien Pharmaceuticals; Financial Interests, Institutional, Funding: BeiGene; Financial Interests, Institutional, Funding: BioAtla, LLC; Financial Interests, Institutional, Funding: Boehringer Ingelheim; Financial Interests, Institutional, Funding: Eli Lilly & Co.; Financial Interests, Institutional, Funding: Hookipa Biotech; Financial Interests, Institutional, Funding: Huya Bioscience International; Financial Interests, Institutional, Funding: IMV, Inc; Financial Interests, Institutional, Funding: Innovent Biologics, Col., Ltd; Financial Interests, Institutional, Funding: Lyvgen Pharma; Financial Interests, Institutional, Funding: MacroGenics; Financial Interests, Institutional, Funding: Medivir AB; Financial Interests, Institutional, Funding: Millennium Pharmaceuticals, Inc.; Financial Interests, Institutional, Funding: Nerviano Medical Sciences; Financial Interests, Institutional, Funding: Neupharma, Inc; Financial Interests, Institutional, Funding: Novartis; Financial Interests, Institutional, Funding: Novocure; Financial Interests, Institutional, Funding: OncoMed Pharmaceuticals; Financial Interests, Institutional, Funding: Parexel International, LLC; Financial Interests, Institutional, Funding: Sellas Life Sciences Group; Financial Interests, Institutional, Funding: Sorcimed Biopharma, Inc.; Financial Interests, Institutional, Funding: Tolero Pharmaceuticals; Financial Interests, Institutional, Funding: National Institutes of Health/National Cancer Institute; Financial Interests, Institutional, Research Grant, P30CA016672 – Core Grant (CCSG Shared Resources): National Cancer Institute/National Institutes of Health; Financial Interests, Full or part-time Employment: MD Anderson - FT. D.G. Pfister: Other, Principal Investigator: Hookipa Pharma; Financial Interests, Advisory Role: Boehringer Ingelheim; Financial Interests, Advisory Role: Celgene; Financial Interests, Advisory Role: Bristol-Myers Squibb; Financial Interests, Advisory Role: Incyte; Financial Interests, Personal, Funding: Boehringer Ingelheim; Financial Interests, Personal, Funding: AstraZeneca; Financial Interests, Personal, Funding: Novartis; Financial Interests, Personal, Funding: MedImmune; Financial Interests, Personal, Funding: Merck; Financial Interests, Personal, Funding: Regeneron; Financial Interests, Personal, Funding: Atara Biotherapeutics; Financial Interests, Personal, Funding: Kura; Financial Interests, Personal, Funding: Esai; Financial Interests, Personal, Funding: Ayala; Financial Interests, Personal, Funding: Plexxikon.

https://doi.org/10.1016/j.annonc.2021.08.1346

962MO A phase I clinical trial on intratumoral injection of autologous CD1c (BDCA-1)+/CD141 (BDCA-3)+ myeloid dendritic cells (myDC) in combination with talimogene laherparepvec (T-VEC) in patients with advanced pretreated melanoma

J.K. Schwarze[1], J. Tijtgat[1], G. Awada[1], L. Cras[2], I. Dufait[3], R. Forsyth[2], I. Van Riet[4], S. Tuyaerts[5], B. Neyns[1]

[1]Department of Medical Oncology, Vrije Universiteit Brussel (VUB), Universitair Ziekenhuis Brussel (UZ Brussel), Brussels, Belgium; [2]Department of Pathology, Vrije Universiteit Brussel (VUB), Universitair Ziekenhuis Brussel (UZ Brussel), Brussels, Belgium; [3]Department of Radiotherapy/Translational Radiation Oncology, Supportive Care and Physics (TROP), Vrije Universiteit Brussel (VUB), Universitair Ziekenhuis Brussel (UZ Brussel), Brussels, Belgium; [4]Stem Cell Laboratory/Department of Clinical Hematology, Vrije Universiteit Brussel (VUB), Universitair Ziekenhuis Brussel (UZ Brussel), Brussels, Belgium; [5]Department of Medical Oncology/Laboratory of Medical and Molecular Oncology (LMMO), Vrije Universiteit Brussel (VUB), Universitair Ziekenhuis Brussel (UZ Brussel), Brussels, Belgium

Background: Intratumoral (IT) myDC play a pivotal role in initiating antitumor immune responses within the tumor microenvironment. IT injection of the oncolytic virus T-VEC may lead to the release of tumor antigens and maturation signals that can be captured and processed by CD1c (BDCA-1)$^+$/CD141 (BDCA-3)$^+$ myDC, thereby reinvigorating the cancer immunity cycle.

Methods: Patients (pts) with ICI-refractory melanoma received IT injections of $\geq$1 non-visceral metastases with T-VEC (10^6 PFU/mL; max 4 mL) on day 1 followed by IT injection of CD1c (BDCA-1)$^+$ (cohort C1) or CD1c (BDCA-1)$^+$/CD141 (BDCA-3)$^+$ myDC (cohort C2) on day 2. Injection of T-VEC (10^8PFU/mL; max 4 mL) was repeated on day 21, and Q2w thereafter. In C1, the number of CD1c (BDCA-1)$^+$myDCs was escalated from $0.5x10^6$, to $1x10^6$, and $10x10^6$ cells. In C2, pts received all isolated CD1c (BDCA-1)$^+$/CD141 (BDCA-3)$^+$ myDCs. Primary objectives were safety and feasibility. Immunohistochemistry (IHC), gene expression profiling (GEP), and multiplexed immunofluorescence (mIF) of baseline and on-treatment biopsies was performed.

Results: 13 pts were enrolled (C1: n=7 [respectively 2, 2, and 3 pts per dose-level of myDC]; C2: n=6). Pts received the predefined dose of myDCs and a median of 6 (range 3-8) T-VEC injections. Most frequent AEs were fatigue in 11 pts (85%), injection-site pain in 9 pts (69%), fever in 8 pts (62%), and chills and flu-like symptoms in 6 pts (46%). There were no G4 or G5 AEs. AEs of special interest were a G3 eosinophilia and a G2 purpuric rash at the injection-site; 2 pts (C1, dose level 3) developed a pathological complete remission that is ongoing at 24 months following treatment initiation. One pt in C2 had an unconfirmed partial response (iRECIST); a mixed response was observed in 2 pts. Responses were observed in both injected and non-injected lesions. In responder pts, infiltration of lymphocytes was observed on IHC. GEP and mIF on biopsies are ongoing.

Conclusions: IT co-injection of CD1c (BDCA-1)$^+$ +/- CD141 (BDCA-3)$^+$ myDC plus T-VEC is feasible, tolerable, and resulted in encouraging early signs of durable antitumor activity in pts with ICI-refractory melanoma.

Clinical trial identification: NCT03747744.

Legal entity responsible for the study: Department of Medical Oncology, Universitair Ziekenhuis Brussel.