VIRTUAL 2020 ESMO congress

1257O

Durability of clinical benefit and biomarkers in patients (pts) with advanced non-small cell lung cancer (NSCLC) treated with AMG 510 (sotorasib)

D.S. Hong[1], Y-J. Bang[2], F. Barlesi[3], G.A. Durm[4], G.S. Falchook[5], R. Govindan[6], G.K. Dy[7], K. Park[8], J.H. Strickler[9], T.F. Burns[10], J. Kim[11], A. Ang[12], J.R. Lipford[13], G. Ngarmchamnanrith[14], A. Anderson[12], B.T. Li[15]

[1] Department of Investigational Cancer Therapeutics, Phase I Clinical Trials Program, The University of Texas M. D. Anderson Cancer Center, Houston, TX, USA, [2] Department of Internal Medicine (Medical Oncology), Seoul National University College of Medicine, Seoul, Republic of Korea, [3] Aix Marseille Université, CNRS, INSERM, CRCM, Assistance Publique Hôpitaux de Marseille, Marseille, Gustave Roussy-Cancer Campus, Villejuif, France, [4] Department of Medicine, Division of Hematology/Oncology, Indiana University School of Medicine, Indianapolis, IN, USA, [5] Department of Medical Oncology, Sarah Cannon Research Institute at HealthONE, Denver, CO, USA, [6] Alvin J Siteman Cancer Center, Washington University School of Medicine, St. Louis, MO, USA, [7] Department of Medicine, Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA, [8] Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea, [9] Department of Medicine, Duke University Medical Center, Durham, NC, USA, [10] Department of Medicine, Division of Hematology/Oncology, University of Pittsburgh Medical Center Hillman Cancer Center, Pittsburgh, PA, USA, [11] Biostatistics, Amgen Inc., Thousand Oaks, CA, USA, [12] Clinical Biomarkers, Amgen Inc., Thousand Oaks, CA, USA, [13] Oncology Research, Amgen Inc., Thousand Oaks, CA, USA, [14] Clinical Development, Amgen Inc., Thousand Oaks, CA, USA[15] Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA

Background

The phase 1 trial of sotorasib, a KRAS^{G12C} inhibitor, demonstrated a favorable safety profile and preliminary antitumor activity in pts with advanced solid tumors harboring *KRAS p.G12C*. Here, we present durability of clinical benefit and biomarker data in pts with NSCLC.

Methods

Key eligibility criteria include *KRAS p.G12C* mutation and prior systemic anticancer treatment (tx). Primary endpoint is safety; key secondary endpoints include objective response rate (ORR), disease control rate (DCR), duration of response (DOR), and progression-free survival (PFS). *KRAS p.G12C* mutant allele frequency (MAF) and PD-L1 level were examined.

Results

As of July 17, 2019, 40 pts with NSCLC (22 female [55.0%], median age: 68.0 years [range: 49-77]) were enrolled. Data cutoff date was March 25, 2020. 31 (77.5%) and 19 pts (47.5%) received ≥ 2 and 3 prior lines of therapy, respectively. Median follow-up was 10.2 (range: 8.3–19.0) months (mos). 3 pts (7.5%) had adverse events leading to discontinuation. There were no dose-limiting toxicities or fatal tx-related adverse events. Median PFS for all pts was 6.9 (range: 1.2–13.9) mos. ORR was 30% (95% CI, 16.56–46.53). DOR ranged from 1.6 (+) to 12.7 mos, with 7 of 12 responders still in response at data cutoff. DCR was 92.5% (95% CI, 79.61–98.43). 18 pts (45.0%) had progressive disease. At data cutoff, 10 pts (25.0%) were on study without disease progression, and 9 pts (22.5%) died. 18 pts (45.0%) (5 partial response (PR), 12 stable disease (SD), 1 progressive disease (PD)) had *KRAS p.G12C* MAF data available. There was no significant association between *KRAS p.G12C* MAF and response (Wilcoxon P = 0.80 for PR vs SD). 11 pts (27.5%) had PD-L1 data available. The median PD-L1 tumor proportion score [TPS] was 3% (range: 1–5) in 2 pts with PR, 0% (range: 0–0) in 8 pts with SD, and 75% (range: 75–75) in the pt with PD (Wilcoxon P = 0.044 for PR vs. SD).

Conclusions

In pts with heavily pretreated NSCLC, durable responses to sotorasib were seen, with the majority of pts achieving disease control leading to a median PFS of 6.9 months. The current limited dataset suggests that neither *KRAS p.G12C* MAF nor PD-L1 expression level predicts response to sotorasib.

Clinical trial identification

NCT03600883.

Editorial acknowledgement

Medical writing support was provided by Liz Leight (Amgen Inc.).

Legal entity responsible for the study

Amgen Inc.

Funding

Amgen Inc.

Disclosure

D.S. Hong: Research grant/Funding (institution), Non-remunerated activity/ies, Other: Bayer; Research grant/Funding (institution): Lilly; Research grant/Funding (institution): Genentech; Honoraria (self), Research grant/Funding (institution): Loxo; Research grant/Funding (institution): Pfizer; Research grant/Funding (institution): Amgen; Research grant/Funding (institution): Mirati; Research grant/Funding (institution): Ignyta; Research grant/Funding (institution): Merck; Research grant/Funding (institution): Daiichi Sanko; Research grant/Funding (institution): Eisai; Research grant/Funding (institution): Adaptimmune; Research grant/Funding (institution): AbbVie; Research grant/Funding (institution): AstraZeneca; Research grant/Funding (institution): BMS; Research grant/Funding (institution): Genmab; Research grant/Funding (institution): Infinity; Research grant/Funding (institution): Kite; Research grant/Funding (institution): Kyowa; Research grant/Funding (institution): MedImmune; Research grant/Funding (institution): Molecular Template; Research grant/Funding (institution): Novartis; Research grant/Funding (institution): Takeda; Honoraria (self): Mirna; Non-remunerated activity/ies, Other: Baxter; Non-remunerated activity/ies, Other: Guidepoint Global; Non-remunerated activity/ies, Other: Oncoresponse; Non-remunerated activity/ies, Other: Janssen; Non-remunerated activity/ies, Other: Molecular Match. Y-J. Bang: Advisory/Consultancy, Research grant/Funding (institution): AstraZeneca; Advisory/Consultancy, Research grant/Funding (institution): Novartis; Advisory/Consultancy, Research grant/Funding (institution): Genentech/Roche; Advisory/Consultancy, Research grant/Funding (institution): MSD; Advisory/Consultancy, Research grant/Funding (institution): Merck Serano; Advisory/Consultancy, Research grant/Funding (institution): Bayer; Advisory/Consultancy, Research grant/Funding (institution): BMS; Advisory/Consultancy, Research grant/Funding (institution): Eli Lilly; Advisory/Consultancy, Research grant/Funding (institution): Taiho; Advisory/Consultancy, Research grant/Funding (institution): Daiich-Sankyo; Advisory/Consultancy, Research grant/Funding (institution): Astellas; Advisory/Consultancy, Research grant/Funding (institution): BeiGene; Advisory/Consultancy, Research grant/Funding (institution): GreenCross; Advisory/Consultancy: Samyang Biopharm; Advisory/Consultancy: Hanmi; Advisory/Consultancy, Research grant/Funding (institution): Genexine; Research grant/Funding (institution): GSK; Research grant/Funding (institution): Pfizer; Research grant/Funding (institution): Boehringer Ingelheim; Research grant/Funding (institution): MacroGenics; Research grant/Funding (institution): Boston Biomedical; Research grant/Funding (institution): FivePrime; Research grant/Funding (institution): Curis; Research grant/Funding (institution): Takeda; Research grant/Funding (institution): Ono; Research grant/Funding (institution): CKD Pharma. F. Barlesi: Honoraria (self), Research grant/Funding (institution), Non-remunerated activity/ies, Principal Investigator for clinical trial: AstraZeneca; Honoraria (self), Research grant/Funding (institution): Bayer; Honoraria (self), Research grant/Funding (institution), Non-remunerated activity/ies, Principal Investigator for clinical trial: Bristol-Myers Squibb; Honoraria (self), Research grant/Funding (institution): Boehringer–Ingelheim; Honoraria (self), Research grant/Funding (institution): Eli Lilly Oncology; Honoraria (self), Research grant/Funding (institution), Non-remunerated activity/ies, Principal Investigator for clinical trial: F. Hoffmann–La Roche Ltd; Honoraria (self), Research grant/Funding (institution): Novartis; Honoraria (self), Research grant/Funding (institution), Non-remunerated activity/ies, Principal Investigator for clinical trial: Merck; Honoraria (self), Research grant/Funding (institution): MSD; Honoraria (self), Research grant/Funding (institution), Non-remunerated activity/ies, Principal Investigator for clinical trial: Pierre Fabre; Honoraria (self), Research grant/Funding (institution): Pfizer; Honoraria (self), Research grant/Funding (institution): Takeda; Research grant/Funding (institution): AbbVie; Research grant/Funding (institution): ACEA; Research grant/Funding (institution): Amgen; Research grant/Funding (institution): Eisai; Research grant/Funding (institution): Genentech; Research grant/Funding (institution): Ipsen; Research grant/Funding (institution): Ignyta; Research grant/Funding (institution): Innate Pharma; Research grant/Funding (institution): Loxo; Research grant/Funding (institution): MedImmune; Research grant/Funding (institution): Sanofi-Aventis .G.A. Durm: Research grant/Funding (institution): Merck; Research grant/Funding (institution): AstraZeneca; Research grant/Funding (institution): Bristol-Myers Squibb; Non-remunerated activity/ies: Amgen. G.S. Falchook: Honoraria (self): Wolters Kluwer; Advisory/Consultancy, Travel/Accommodation/Expenses: FujiFilm; Travel/Accommodation/Expenses: Bristol-Myers Squibb; Travel/Accommodation/Expenses: Sarah Cannon Research Institute; Speaker Bureau/Expert testimony: Total Health Conferencing; Research grant/Funding (institution): 3-V Biosciences; Research grant/Funding (institution): AbbVie; Research grant/Funding (institution): ADC Therapeutics; Research grant/Funding (institution): Aileron; Research grant/Funding (institution): American Society of Clinical Oncology; Research grant/Funding (institution): Amgen; Research grant/Funding (institution): ARMO; Research grant/Funding (institution): AstraZeneca; Research grant/Funding (institution): BeiGene; Research grant/Funding (institution): Bioatla; Research grant/Funding (institution): Biothera; Research grant/Funding (institution): Celldex; Research grant/Funding (institution): Celgene; Research grant/Funding (institution): Ciclomed; Speaker Bureau/Expert testimony: Rocky Mountain Oncology Society ; Research grant/Funding (institution): Curegenix; Research grant/Funding (institution): Curis; Research grant/Funding (institution): Cyteir; Research grant/Funding (institution): Daiichi; Research grant/Funding (institution): DelMar; Research grant/Funding (institution): eFFECTOR; Research grant/Funding (institution): Eli Lilly; Advisory/Consultancy, Research grant/Funding (institution), Travel/Accommodation/Expenses: EMD Serono; Research grant/Funding (institution): Epizyme, Exelixis, Fujifilm, Genmab, GlaxoSmithKline, Hutchison MediPharma, Ignyta, Incyte, Jacobio, Jounce, Kolltan, Loxo, MedImmune, Millennium, Merck, miRNA Therapeutics, National Institutes of Health, Novartis, OncoMed, Oncorus; Research grant/Funding (institution): Oncothyreon, Poseida, Precision Oncology, Prelude, Regeneron, Rgenix, Ribon, Strategia, Syndax, Taiho, Takeda, Tarveda, Tesaro, Tocagen, Turning Point Therapeutics, U.T. MD Anderson Cancer Center, Vegenics, Xencor. K. Park: Advisory/Consultancy: Amgen. J.H. Strickler: Advisory/Consultancy, Research grant/Funding (institution): Amgen. T.F. Burns: Advisory/Consultancy: Novartis; Advisory/Consultancy: Blueprint Medicine; Advisory/Consultancy: Thermo Fisher Scientific. J. Kim: Shareholder/Stockholder/Stock options, Full/Part-time employment: Amgen. A. Ang: Shareholder/Stockholder/Stock options, Full/Part-time employment: Amgen. J.R. Lipford: Shareholder/Stockholder/Stock options, Full/Part-time employment: Amgen. G. Ngarmchamnanrith: Shareholder/Stockholder/Stock options, Full/Part-time employment: Amgen. A. Anderson: Shareholder/Stockholder/Stock options, Full/Part-time employment: Amgen. B.T. Li: Advisory/Consultancy, Research grant/Funding (institution): Genentech/Roche; Advisory/Consultancy: Thermo Fisher Scientific; Advisory/Consultancy, Research grant/Funding (institution): Guardant Health; Advisory/Consultancy, Research grant/Funding (institution): Hengrui Therapeutics; Advisory/Consultancy: Mersana Therapeutics; Advisory/Consultancy, Research grant/Funding (institution): Eli Lilly; Travel/Accommodation/Expenses: Resolution Bioscience; Research grant/Funding (institution), Travel/Accommodation/Expenses: MORE Health; Research grant/Funding (institution): Amgen; Research grant/Funding (institution): Daiichi Sankyo; Research grant/Funding (institution): AstraZeneca; Research grant/Funding (institution): BioMedValley Discoveries; Research grant/Funding (institution): Illumina; Research grant/Funding (institution): GRAIL. All other authors have declared no conflicts of interest.