# 1616O - Multicenter, nonrandomized, open-label Phase 1b study of FP-1039/GSK3052230 with chemotherapy: results in malignant pleural mesothelioma (MPM)


## Background

Fibroblast growth factor (FGF) signaling has a fundamental role in cancer development and tumor maintenance. FP-1039/GSK3052230 is a soluble decoy receptor that sequesters FGFs, including FGF2, blocking their ability to bind to and activate FGFRs, particularly FGFR1. This unique mechanism of action should avoid the on-target toxicities associated with small molecule pan FGFR kinase inhibitors, such as hyperphosphatemia and retinal, nail, and skin changes. MPM remains a disease with poor prognosis and few effective therapies, and preclinical models of MPM are particularly sensitive to inhibition of FGF/FGFR signaling by FP-1039/GSK3052230.

## Methods

Herein, the analysis of patients with untreated, unresectable MPM is reported. The MPM arm of the study evaluated the safety and efficacy of FP-1039/GSK3052230 (IV weekly) in combination with standard pemetrexed+cisplatin. The study design involved dose escalation until MTD followed by a cohort expansion phase. Endpoints included safety, overall response rate by modified RECIST 1.1, disease control rate (DCR), PFS, and exploratory translational objectives.

## Results

As of the cutoff date of 17 Mar 2017, 36 patients were dosed at 10, 15 and 20 mg/kg doses of FP-1039/GSK3052230. Three DLTs were observed at 20 mg/kg but none occurred at 15 mg/kg; therefore, MTD was declared at this dose. Most common related adverse events (all grades) were: nausea (56%) decreased appetite (36%), fatigue (33%), and infusion reaction (33%). The confirmed objective response rate (ORR) of all evaluable patients at or below the MTD was 48% (13/27 PRs), with disease control rate (DCR) of 100%. The median PFS was 7.4 months. As of 8 May 2017, six patients stayed on the study for over 1 year, of which 3 were still ongoing. Results of exploratory biomarker analyses will also be presented.

## Conclusions

The MTD of FP-1039/GSK3052230 (15 mg/kg) in combination with pemetrexed+cisplatin in MPM was well tolerated, and durable responses were observed. Importantly, AEs associated with small-molecule pan FGFR kinase inhibitors were not observed, as predicted by the unique mechanism of action of this drug. Study sponsored by GSK; clinical trial information: NCT01868022.


## Clinical trial identification

NCT01868022

## Legal entity responsible for the study

GlaxoSmithKline


## Funding

GlaxoSmithKline


## Disclosure

D.A. Fennell: Advisory Board/consultant – Astra Zeneca, BMS, Bayer, Boehringer Ingelheim, Clovis, Roche, Eli Lilly, MSD H.L. Kindler: Advisor: Aduro; AZ; Bayer; Celgene; Genentech/Roche; Gilead; GSK; MedImmune; Merck; Plexxikon; Verastem. Grants: AB Science; Aduro; Astellas Pharma; AZ; Bayer; Celgene; GSK; Incyte; MedImmune; Merck; Verastem. Expert Testimony: Aduro S. Viteri: Grants: AbbVie, ARIAD, Astex, AZ, BI, Clovis, CytRx, Daiichi

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