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FP1039/GSK3052230 With Chemotherapy in Squamous NSCLC or MPM Patients With Deregulated Fibroblast Growth Factor (FGF) Pathway

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P. GARRIDO DISCLOSURES:

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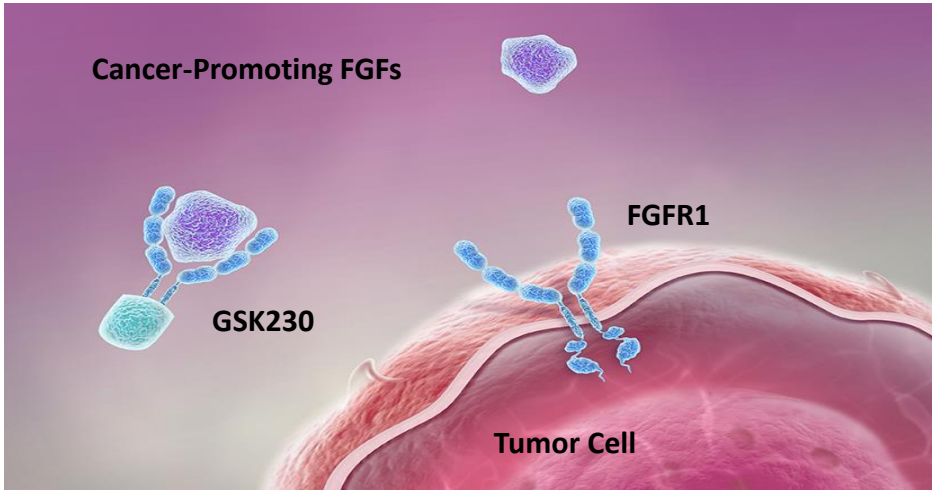
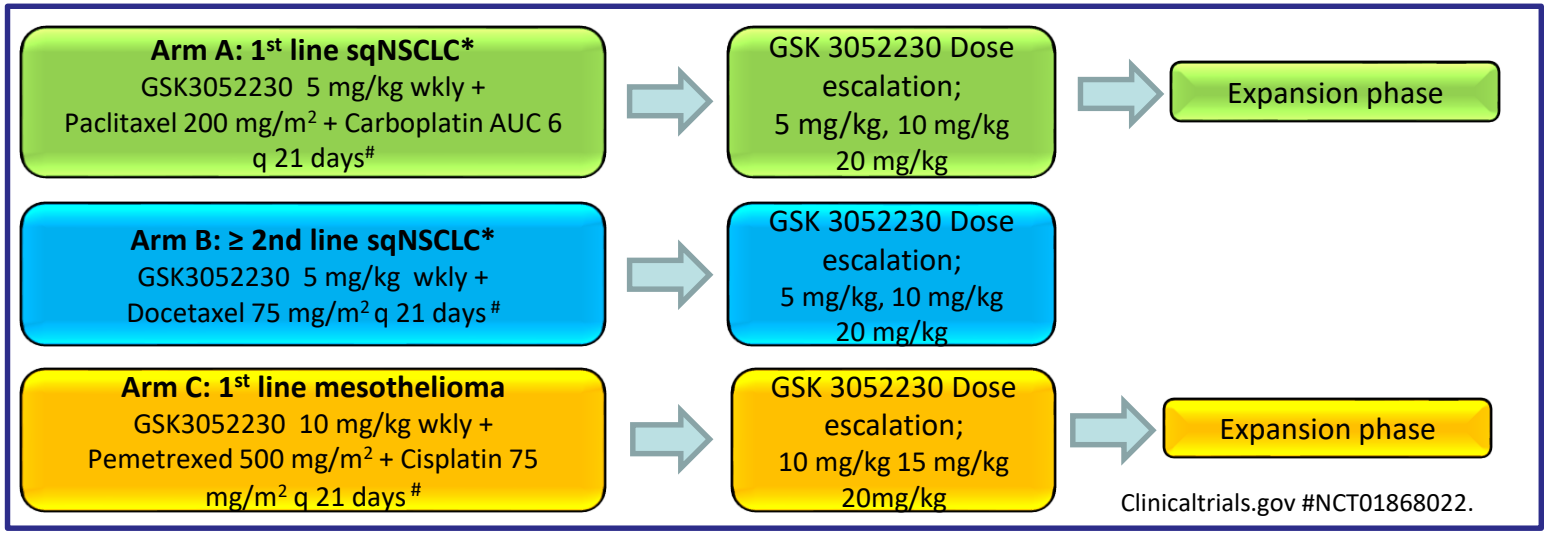
GSK3052230 Selectively Blocks FGFR1 Ligands



Tumor cell growth
Tumor cell survival

- Selectively blocks cancer-promoting FGFs that bind to FGFR1
- Avoids retinal detachment, hyperphosphatemia, mucositis, and nailbed changes seen with small molecule TKIs
- MPM frequently overexpress FGF2 and ~20% of sqNSCLC show *FGFR1* amplification that is associated with diminished survival

FGF117360: Study Design



Primary objectives:

- Evaluate the maximum tolerated dose (MTD) or maximum feasible dose (MFD) of GSK3052230 in combination with chemotherapy
- Safety and tolerability of GSK3052230 (Dose limiting toxicities [DLTs], rate and severity of adverse events)

Global study: 34 centers in 8 countries (USA, UK, Russia, Spain, France, Netherlands, Denmark, Belgium)

**FGFR1* gene amplification required. # Regimens as of Socinski et al, 2012 (Arm A); Hanna et al, 2004 (B); Vogelzang et al, 2003 (C).

Treatment Summary and Primary Objective

Data as of 05Aug2015

- 176 patients with 1L or 2L+ sqNSCLC tested centrally for *FGFR1* amplification; 34 (19%) amplified
- 44 patients enrolled into the study: 18 Arm A, 7 Arm B, 19 Arm C
- Three DLTs
  - All were reported in mesothelioma patients (Arm C, dose level = 20 mg/kg)
  - NCI CTCAE Gr 5 bowel perforation/ischemia; Gr 3 elevated creatinine levels; Gr 3 infusion reaction
- Arm A: an MTD was not identified; 20 mg/kg IV weekly GSK3052230 was considered MFD
- Arm B: dose escalation is ongoing
- Arm C: MTD was established at 15 mg/kg IV weekly GSK3052230

Treatment-emergent adverse events regardless of causality that occur in >33% of patients of any arm

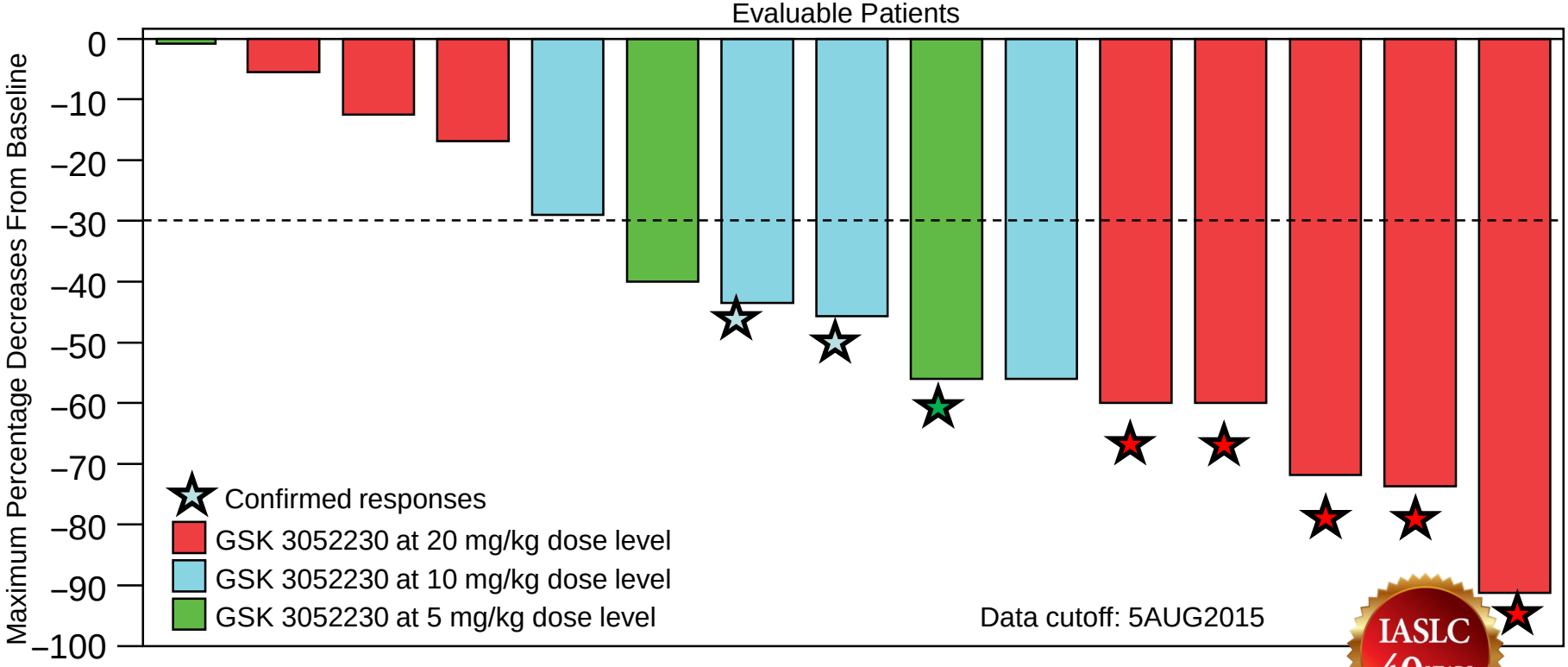
Adverse Event	Arm A (n=18)		Arm B (n=7)		Arm C (n=19)	
	All grades	Grade 3-4	All grades	Grade 3-4	All grades	Grade 3-4
Neutropenia	**11 (61%)**	8 (44%)	2 (29%)	0	2 (11%)	1 (5%)
Anemia	**6 (33%)**	1 (6%)	0	0	4 (21%)	1 (5%)
Constipation	**7 (39%)**	0	2 (29%)	0	6 (32%)	0
Diarrhea	**7 (39%)**	2 (11%)	2 (29%)	1 (14%)	5 (26%)	0
Nausea	**6 (33%)**	0	2 (29%)	0	**12 (63%)**	0
Vomiting	4 (22%)	0	1 (14%)	0	**7 (37%)**	0
Decreased appetite	5 (28%)	0	1 (14%)	0	**9 (47%)**	0
Pyrexia	4 (22%)	0	**3 (43%)**	0	3 (16%)	0
Fatigue	**6 (33%)**	1 (6%)	2 (29%)	0	6 (32%)	1 (5%)
Asthenia	5 (28%)	2 (11%)	1 (14%)	0	**7 (37%)**	0
Alopecia	**7 (39%)**	0	**3 (43%)**	1 (14%)	0	0
Infusion related reaction	3 (17%)	0	1 (14%)	0	**7 (37%)**	1 (5%)

Preliminary Efficacy

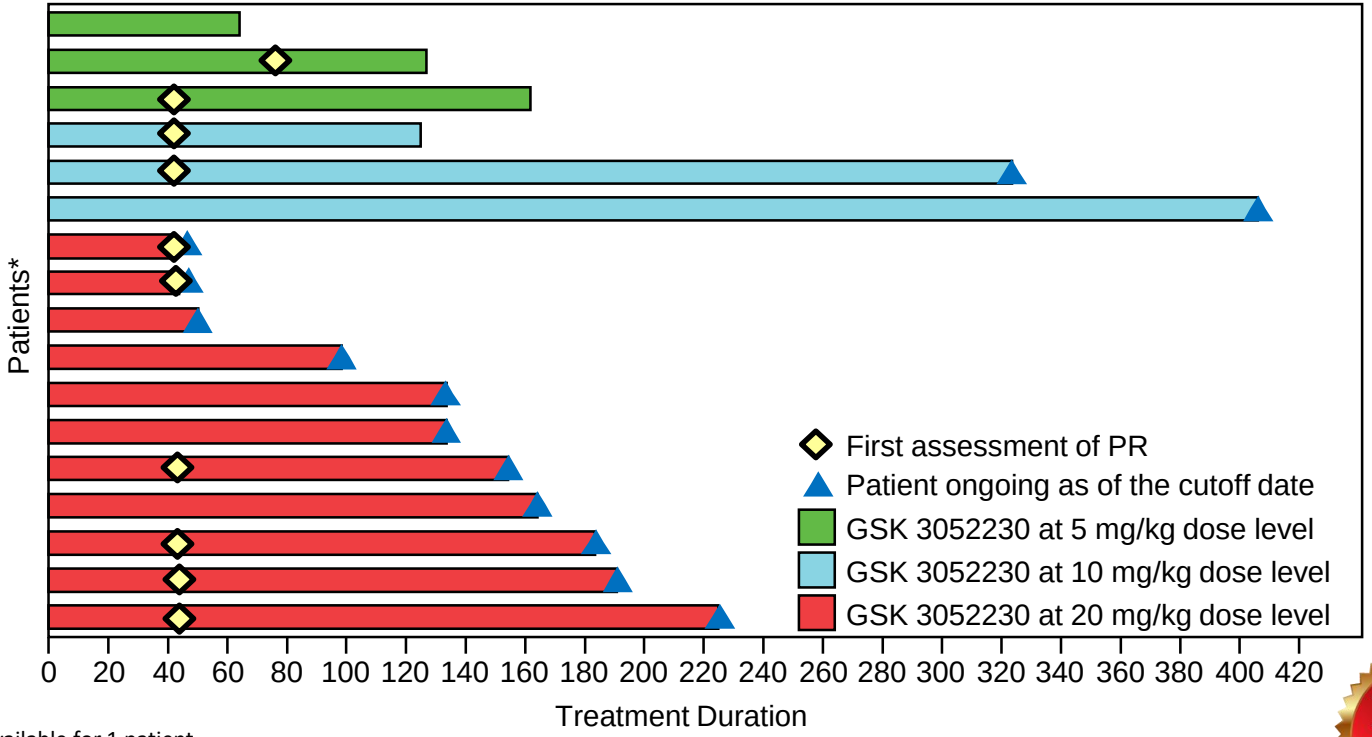
Best tumor response	Arm A (1L sqNSCLC): Paclitaxel + carboplatin +GSK3052230 (n=18)	Arm B (2L+ sqNSCLC): Docetaxel + GSK3052230 (n=7)	Arm C (1L MPM): Pemetrexed + cisplatin + GSK3052230 (n=19)
Partial response	10*	0	3
Stable disease	3	4	5
Progressive disease	2	1	1
Not evaluable	3	2	10
ORR	55%	0%	16%
Disease Control Rate (CR +PR +SD)	72%	57%	42%

*Includes 2 unconfirmed responses. Not evaluable includes subjects without post-baseline scan, eg enrolled recently.

Tumor Reduction in Arm A (1L sqNSCLC)



Duration of Treatment in Arm A (1L sqNSCLC)



* Data cutoff: 5AUG2015;
data were incomplete/not available for 1 patient.

TAKE HOME MESSAGES

- GSK3052230 is generally well tolerated in combination with chemotherapy (CT)
- 3 DLTs for GSK3052230 in combination with CT were found at dose of 20 mg/kg IV weekly only in Arm C; 20 mg/kg was considered MFD in Arm A and an MTD was established at 15 mg/kg in Arm C
- The most common toxicities were neutropenia and nausea; toxicities typically associated with small-molecule FGFR inhibitors namely hyperphosphatemia and retinal, nail, and skin changes, were not observed
- Approximately 20% of patients with sqNSCLC tested positive for *FGFR1* gene amplification
- In Arm A, overall response rate was 55% and disease control rate 72%, with good durability of response
- The initial activity and safety profile of GSK3052230 warrant further study

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