

Abstract #467

Phase II study of ganetespib, an hsp-90 inhibitor, in patients with refractory metastatic colorectal cancer.

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Background: To evaluate the safety and efficacy of ganetespib, a heat shock protein 90 (Hsp90) inhibitor, as monotherapy in patients with refractory metastatic colorectal cancer.

Methods: A phase II study utilizing a two-stage design was performed in which patients received Ganetespib 200 mg/m² intravenously (IV) one time per week for three weeks followed by a one week break. Patients underwent pre and 48 hour post treatment tumor biopsies. Immunohistochemistry (IHC) was performed for p/Erk, CyclinD1, p/Akt, HIF-1a, VEGFr2, p70S6 and Hsp70. Archived and pre dose biopsy tissue was utilized for KRAS, BRAF and PIK3CA genotyping using a Sequenom platform.

Results: Fifteen patients were treated (median age 58, range 44-79). There were no responders. Two patients had stable disease lasting 31 and 23 weeks. The most frequent grade 1/2 toxicities were diarrhea, fatigue, nausea/vomiting and elevated transaminases (Table). These complications did not result in any treatment interruption. The most frequent grade 3 adverse events were diarrhea (12%), fatigue (24%), and elevated AST (12%) and Alk phos (29%). Three (20%) patients required dose reductions, 1 grade 3 AST, 1 grade3 ALT and 1 grade 3 fatigue.

Conclusions: This was the first study of an Hsp90 inhibitor in colorectal cancer. Ganetespib treatment did not produce tumor responses when administered as a single agent in refractory metastatic colorectal cancer with this dosing regimen. Overall the drug was well tolerated and the toxicity profile was minimal. Ganetespib may be used in combination in future studies. Correlative IHC analyses will be presented.

Grade 1/2 and 3 toxicities (total patients n = 17, %).

	Grade 1/2	Grade 3
Diarrhea	14 (82%)	2 (12%)
Fatigue	9 (53%)	4 (24%)
Nausea	9 (53%)	0
Vomiting	11 (65%)	1 (6%)
Anorexia	7 (41%)	0
Headache	4 (24%)	0
Dehydration	0	1 (6%)
Alk phos (↑)	8 (47%)	0
AST (↑)	9 (53%)	2 (12%)
ALT (↑)	12 (70%)	1 (6%)
Amylase (↑)	5 (29%)	0
Bilirubin	6 (35%)	0
Hypokalemia	0	1 (6%)
Hyponatremia	0	3 (18%)
