96P AXL has a prognostic role in metastatic colorectal cancer (mCRC) and is a predictive biomarker of lack of efficacy of chemotherapy (CT) + cetuximab in RAS wild type (WT) patients (pts)

C. Cardone[1], B. Blauensteiner[2], V. Moreno-Viedma[2], M.C. Paul[2], G. Martini[1], P.P. Vitiello[1], D. Ciardiello[1], C. Borrelli[1], L. Poliero[1], P. Vitale[1], N. Zanaletti[1], V. Famiglietti[1], A.M. Rachiglio[3], D. Rizzi[4], E. Maiello[5], T.P. Latiano[5], N. Normanno[3], M. Sibilia[2], F. Ciardiello[1], E. Martinelli[1]

[1]Medical Oncology, Università degli Studi della Campania Luigi Vanvitelli, Naples, Italy, [2]Institute of Cancer Research, Medical University of Vienna, Vienna, Austria, [3]Cell Biology and Biotherapy Unit, National Cancer Institute 'Fondazione Giovanni Pascale', Naples, Italy, [4]Clinical Research, GOIM Trial Office, Bari, Italy, [5]Oncology, Hospital Casa Sollievo della Sofferenza-IRCCS, San Giovanni Rotondo, Italy

Background: AXL expression promotes tumour growth, angiogenesis, epithelial to mesenchymal transition (EMT), resistance to CT and targeted agents. AXL is overexpressed in CRC. We aimed to evaluate AXL expression in mCRC pts and to correlate it with clinical outcomes.

Methods: AXL expression was assessed by immunohistochemistry in tumor samples of a consecutive series of 109 mCRC pts (75 RAS mutant and 34 RAS WT) treated at our Institution and 68 mCRC RAS WT pts enrolled in CAPRI-GOIM trial. Pts received a first line treatment according to RAS status: RAS mutant pts (n = 75) received CT + anti-angiogenic drugs, RAS WT pts (n = 102) CT + cetuximab.

Results: AXL stained positively in 20/177 samples with different intensity: 13 weak, 5 moderate, 2 intense. In RAS WT cohort 9/102 cases (9%) were positive while in RAS mutant 11/75 (15%). Tumor stroma was assessable in 166 samples. AXL expression was high (moderate + intense) in 47/96 (49%) RAS WT and in 28/70 (40%) RAS mutant cases. No significant correlation was found between AXL expression and clinico-pathological features. In RAS WT cohort, AXL positive pts had a significantly worse median PFS [4.3 m (CI95% 3.2-5.5) vs 12.1 m (CI95% 11.0-13.3) p = 0.001], in RAS mutant no impact on PFS was observed. AXL expression in tumor was a negative prognostic factor in both cohorts although statistical significance was reached only in RAS mutant [median OS: 30.2 m (CI95% 18.4-42.0) vs 20.1 m (CI95% 10.6-29.6) p = 0.007]. Intriguingly, high AXL expression in stroma correlated with lower median OS in both cohorts (Table).

Conclusions: AXL, marker of EMT phenotype, might represent an additional predictive biomarker of lack of efficacy in RAS WT mCRC pts treated with CT + cetuximab. Moreover, its expression in tumor and stroma might have a negative prognostic relevance in mCRC. Targeting AXL could overcome resistance to anti-epidermal growth factor receptor and represent a novel therapeutic strategy in mCRC.

Clinical trial identification: CAPRI-GOIM Trial = EudraCT 2009-014041-81.

Legal entity responsible for the study: Department of Precision Medicine, Università degli Studi della Campania "Luigi Vanvitelli".

Funding: Grant by AIRC = MFAG-2015-ID: 7778.

Disclosure: All authors have declared no conflicts of interest.

Table: 96P

Cohort	Median OS (months - CI95%) AXL expression in tumor		Median PFS (months - CI95%) AXL expression in tumor		Median OS (months - CI95%) AXL expression in stroma		Median PFS (months - CI95%) AXL expression in stroma	
N (tumor) / N (stroma)	AXL positive	AXL negative	AXL positive	AXL negative	AXL high	AXL low	AXL high	AXL low
Overall population N = 177 / N = 166	20.1 (12.8-27.4)	36.5 (30.6-42.3) p = 0.02	-	-	25.3 (21.4-29.3)	46.4 (34.6-58.2) p = 0.003	-	-
RAS WT (CT + cetuximab) N = 102 / N = 96	23.0 (0.0- 63.3)	39.8 (30.2– 49.4) p = 0.66	4.3 (3.2- 5.5)	12.1 (11.0– 13.3) p = 0.001	28.8 (17.4- 40.1)	47.7 (29.7– 65.7) p = 0.021	10.7 (8.4- 13.0)	12.4 (9.6– 15.2) p = 0.06
RAS mutant (CT + anti-angiogenic) N = 75 / N = 70	20.1 (10.6- 29.6)	30.2 (18.4- 42.0) p = 0.007	8.9 (5.4- 12.4)	9.1 (7.6- 10.7) p = 0.444	24.2 (18.2- 30.1)	37.7 (16.8- 58.6) p = 0.026	8.9 (6.1- 11.8)	8.6 (7.3- 10.0) p = 0.53