111: A Phase 1b Study of Navicixizumab plus FOLFIRI in 2nd line Metastatic Colorectal Cancer Patients

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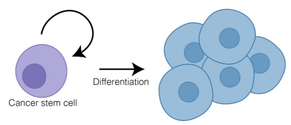
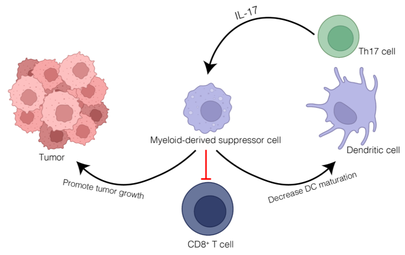
Background

- Navicixizumab is an anti-delta-like ligand 4 (DLL4)/vascular endothelial growth factor (VEGF) bispecific antibody
- DLL4 blockade leads to:

Cancer stem cell differentiation



Repolarization of the immune microenvironment



Methods

- We conducted a phase 1b single-arm dose-escalation study combining navicixizumab with FOLFIRI or FOLFOX as second-line treatment for patients with metastatic colorectal cancer (CRC)
- Primary endpoint: maximum tolerated dose of navicixizumab in combination with FOLFIRI or FOLFOX

Results

- A total of 15 patients received navicixizumab + FOLFIRI
  - 3 patients in 3 mg/kg dose escalation cohort
  - 2 patients in 4 mg/kg dose escalation cohort
  - 10 patients in 3 mg/kg dose expansion cohort
- No DLTs were observed
- Median duration of navicixizumab therapy: 127 days
- Study was stopped early to focus the development of navicixizumab on ovarian cancer

Navicixizumab plus FOLFIRI shows promising disease control rate in second-line colorectal cancer

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Overall Tumor Response (ITT population)

	Navicixizumab 3 mg/kg Q2W (N = 3) n (%)	Navicixizumab 4 mg/kg Q2W (N = 2) n (%)	Navicixizumab 3 mg/kg Q2W (Expansion) (N = 10) n (%)	Navicixizumab Overall (N = 15) n (%)
Best Overall Response				
Complete Response	0	0	0	0
Partial Response	1 (33.3)	0	2 (20.0)	3 (20.0)
Stable Disease	2 (66.7)	2 (100)	7 (70.0)	11 (73.3)
Progressive Disease	0	0	1 (10.0)	1 (6.7)
Not Evaluable	0	0	1 (10.0)	1 (6.7)
Objective Response Rate (CR or PR)	33.3	0	2 (20.0)	20
Disease Control Rate (CR or PR or SD)	100	100	9 (90.0)	93.3

Summary of Treatment-related TEAEs (≥ CTCAE Grade 3) (Safety population)

	CTCAE Grade	Navicixizumab 3 mg/kg Q2W (N = 3) n (%)	Navicixizumab 4 mg/kg Q2W (N = 2) n (%)	Navicixizumab 3 mg/kg Q2W (Expansion) (N = 10) n (%)	Navicixizumab Overall (N = 15) n (%)
Subjects with at least one treatment-related ≥ Grade 3 TEAE		3 (100)	2 (100)	10 (100)	15 (100)
Grade 3		3 (100)	1 (50)	4 (40)	8 (53)
Grade 4		0	0	1 (10)	1 (7)
Grade 5		0	0	1 (10)	1 (7)
Blood and lymphatic system disorders					
Neutropenia	3	1 (33)	0	0	1 (7)
Cardiac disorders					
Cardio-respiratory arrest	5	0	0	1 (10)	1 (7)
Right ventricular failure	3	0	0	1 (10)	1 (7)
Gastrointestinal disorders					
Diarrhea	3	0	1 (50)	0	1 (7)
Mesenteric vein thrombosis	3	1 (33)	0	0	1 (7)
Proctalgia	3	1 (33)	0	0	1 (7)
Rectal perforation	4	0	0	1 (10)	1 (7)
Hepatobiliary disorders					
Cholecystitis	3	1 (33)	0	0	1 (7)
Gallbladder perforation	3	1 (33)	0	0	1 (7)
Injury, poisoning, and procedural complications					
Wound	3	0	0	1 (10)	1 (7)
Investigations					
B-type natriuretic peptide increased	3	1 (33)	0	2 (20)	3 (20)
Electrocardiogram T wave inversion	3	0	1 (50)	0	1 (7)
Respiratory, thoracic, and mediastinal disorders					
Pulmonary hypertension	3	0	0	1 (10)	1 (7)
Vascular disorders					
Hypertension	3	0	0	3 (30)	3 (20)