ECD International Medical Symposium
Paris, France
September 15, 2016

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

Encouraging activity of MEK inhibitor trametinib in patients with Erdheim-Chester disease irrespective of *BRAF* mutation status

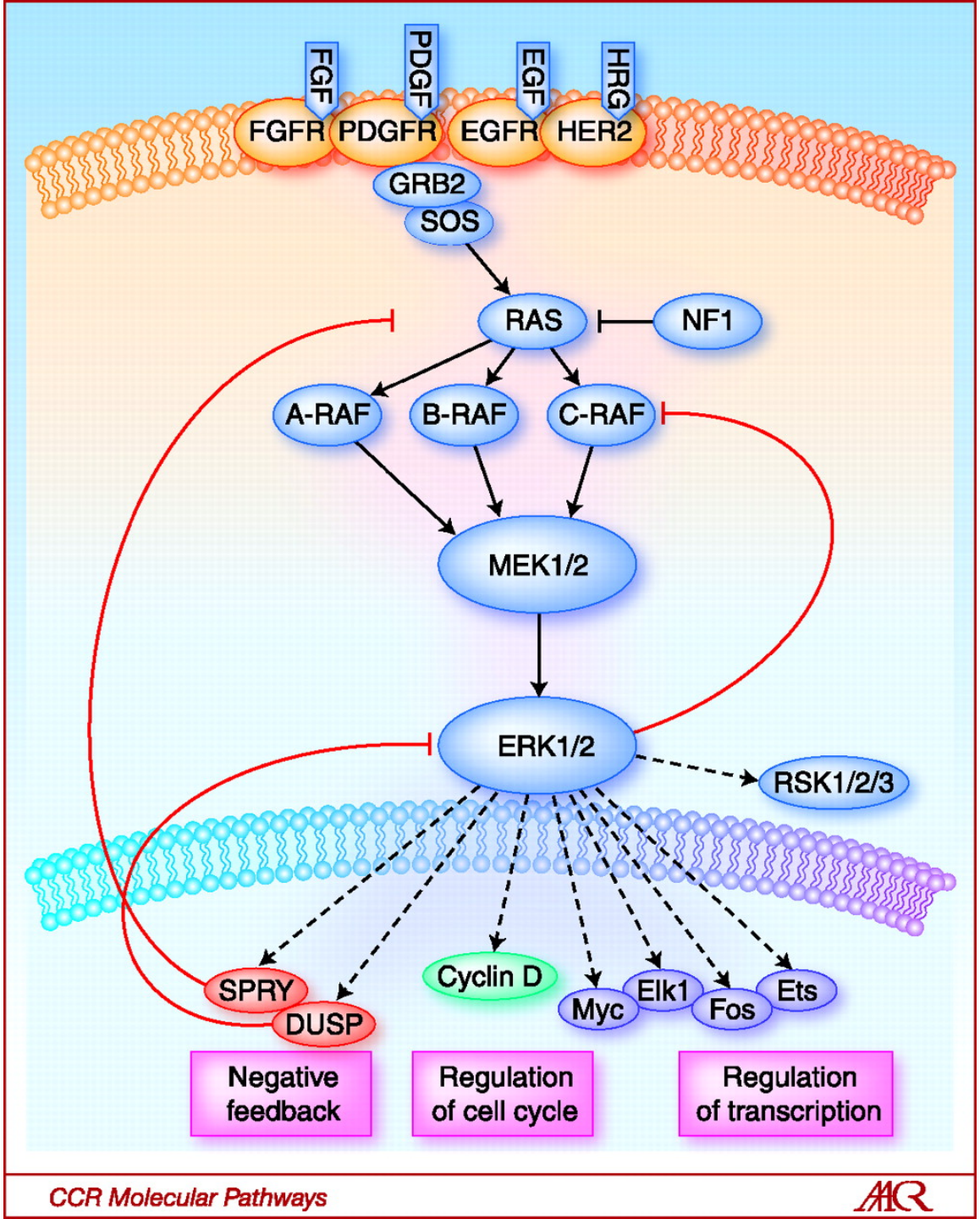
Filip Janku, Tamara G. Barnes

Investigational Cancer Therapeutics
(Phase I Clinical Trials Program)
MD Anderson Cancer Center
Houston, TX

Bench to Bedside & Back

Rationale

- *BRAF* V600E mutation is the most prevalent molecular abnormality present in about 60% of patients Erdheim-Chester disease (ECD)
- ECD patients without *BRAF* V600E mutation often have other molecular aberrations in the MAPK pathway
- We hypothesize that activation of the MAPK pathway is a hallmark feature of ECD irrespective of molecular profile
- MEK inhibitor trametinib is an effective inhibitor of the MAPK pathway signaling



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Methods

- Population
  - Patients with unknown or pending molecular testing
  - Patients without targetable molecular alteration
- Molecular testing
  - Tumor tissue targeted next generation sequencing (NGS)
  - Plasma cell-free DNA targeted NGS
- Treatment
  - Trametinib, an oral inhibitor of MEK1/ 2 kinase at the dose of 1 mg daily (50% of FDA approved dose for melanoma)

Patients

Patient No.	Age/Sex	Disease involvement	Prior therapy	Treatment	Molecular testing
MDA20	42/male	Skin, bones	anakinra; everolimus and anakinra	**Continues on trametinib 1mg daily for 4+ month with mild symptom improvement. Anakinra was added at month 2**	None (targeted plasma cfDNA NGS and plasma BRAF PCR)
MDA22	42/male	Skin, bones, neurological symptoms	anakinra; everolimus and anakinra	**Trametinib 1mg daily for 4 months. His symptoms improved dramatically, but did not resolve, therefore the dose was increased to 1.5mg and he continues on increased dose for 2 months with further improvement**	None (targeted plasma cfDNA NGS and plasma BRAF PCR)

Patients

Patient No.	Age/Sex	Disease involvement	Prior therapy	Treatment	Molecular testing
MDA23	60/male	Orbits, cardiac, kidneys, bones, sinuses, vertebral arteries	Continues on trametinib 1mg daily for 8+ months with significant symptomatic and radiographic improvement. Dabrafenib was not added because of prolonged QTc	**Continues on trametinib 1mg daily for 8+ months with significant symptomatic and radiographic improvement. Dabrafenib was not added because of prolonged QTc**	BRAFV600E
MDA25	48/male	Pituitary, aorta, lungs, bones, kidneys, abdomen	Trametinib 1mg daily for 3 months with mild symptom improvement, the dose increased to 1.5mg and added dabrafenib 75mg BID	Trametinib 1mg daily for 3 months with mild symptom improvement, the dose increased to 1.5mg and added dabrafenib 75mg BID	BRAFV600E

CONCLUSIONS

- ❑ Trametinib can be an alternative in symptomatic patients without druggable alterations or unknown molecular profile

- ❑ These preliminary results need to be confirmed in larger series