Identification of potential molecular biomarkers for response of soft tissue sarcoma to eribulin: Translational results of EORTC trial 62052.

Authors:

Agnieszka Wozniak, Erik A.C. Wiemer, Herman Burger, Joke Allemeersch, Rudy van Eijnden, Ron H.J. Mathijssen, Stefan Sleijfer, Marcel Smid, Giuseppe Floris, Sandrine Marreaud, Axelle Nzokirantevye, Raf Sciot, Patrick Scho"ski; Laboratory of Experimental Oncology and Department of General Medical Oncology, KU Leuven and University Hospitals, Leuven, Belgium; Erasmus MC-Daniel den Hoed Cancer Center, Rotterdam, Netherlands; Nucleomics Core, VIB, Leuven, Belgium; Department of Medical Oncology, Erasmus University Medical Center, Rotterdam, Netherlands; Erasmus MC, Department of Medical Oncology and Cancer Genomics Netherlands, Rotterdam, Netherlands; Department of Pathology, KU Leuven and University Hospitals, Leuven, Belgium; European Organisation for Research and Treatment of Cancer (EORTC), Brussels, Belgium

Research Funding:

Background:

The phase II study EORTC 62052 demonstrated potential antitumor activity of eribulin, a tubulin-interacting cytotoxic agent, which is a synthetic analogue of the natural compound halichondrin B, in patients with various subtypes of metastatic soft tissue sarcoma (STS) including leiomyo- (LMS) and adipocytic (ADI) sarcomas, but not synovial sarcomas (SYN) and other sarcoma histotypes (OTH) (Schöffski P et al. Lancet Oncol. 2011;12:1045). In addition to histotypes, we aimed to identify potential biomarkers responsible for eribulin sensitivity or resistance to eribulin using gene expression and miRNA profiling.

Methods:

From 68 consenting patients archived tumor tissue was collected, including 22 LMS, 15 ADI, 10 SYN and 21 OTH sarcoma histotypes. Total RNA was isolated from 65 samples and analyzed using GeneChip Human Exon ST Array (for mRNA expression) and Taqman Low Density Array (for miRNA). Progression free survival (PFS) at week 12 (RECIST 1.0) was the primary endpoint of the clinical trial and used for correlative studies. Eighteen out of 56 (32.1%) evaluable patients in this analyzed subset had non progressive disease at week 12 ("responders").

Results:

Overall expression of 62 transcripts including *ALS2CR11* (uncorrected p<0.001) and 26 miRNAs (p<0.05) differed significantly between non-responders and responders. Additional transcripts and miRNAs were identified when considering the different histological groups (Table).

Conclusions:

The level of (mi)RNA expression in soft tissue sarcoma samples may predict response of soft tissue sarcoma to eribulin. Further validation studies are required.

	Number of differentially expressed transcripts			Number of differentially expressed miRNAs		
	Downregulated*	Upregulated*	Potential biomarker	Downregulated*	U-regulated*	Potent biomarker
All STS	20	42	ALS2CR11	18	8	miR-192 cluster
Subtypes**						
ADI	58	500	MYLK3	8	0	miR-106b
LMS	11	19	SLC8A1	6	2	miR-146a, 1271, 590-3, 29b-2
OTH	66	93	IGF2, COL1A2	1	0	miR-1

***In responders. ** SYN subgroup not taken into account as only one patient reached PFS at 12 weeks.**

This material on this page is ©2013 American Society of Clinical Oncology, all rights reserved. Licensing available upon request. For more information, please contact licensing@asco.org.