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Short Communication

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Drug measurements at the pharmacological target site for individualized pediatric cancer treatment

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Abstract:

Cancer drug resistance is a consequence of a complex, multidimensional interplay between tumor, its environment and thernhost. Drugs are oft en assumed to distribute relatively homogeneously from plasma to tumor tissues. However, distributionrnof drug in tumors is highly variable and may not correlate with dose or plasma concentrations. Solid tumors are characterizedrnby a complex and unique microenvironment that consists of infi ltrating immune cells, low pH, dense interstitial matrix, highrninterstitial pressure, and abnormal blood and lymphatic vascular structures. Overexpression of drug effl ux transporters suchrnas P-glycoprotein (MDR1/ABCB1), breast cancer resistance protein (BCRP/ABCG2), and transporters of the multidrugrnresistance-associated protein subfamily (MRP/ABCC) may also limit drug penetration in cancer cells or other (off) targetrncells. Variability in these factors among cancer types may be a contributing factor why translation from adults to pediatricrnpatients often fails. Until recently, assessment of spatial drug distribution in cancer cells or other target cells and clinical implementation ofrnthese data was limited by technical challenges. New technologies such mass spectrometric and radiolabeled drug imagingrnaddress these challenges and illustrate the promise of applying imaging for optimal development and precision dosing andrncan be directly applied in pediatric dosing studies. In the presentation we will present an overview of our current knowledgernof the association between drug penetration in plasma and target (cancer) cells and their eff ect on tumor response and discussrnapproaches for performing measurements of drug uptake at the pharmacological target site in pediatric patients.

Biography:

Imke H. Bartelink completed her PharmD and PhD in clinical pharmacology in pediatric hematopoietic cell transplantation from the Utrecht Medical Center in Utrecht, The Netherlands and postdoctoral studies in integrative pharmacology from the University of California, San Francisco (UCSF). Currently, Dr. Bartelink is in the Clinical Pharmacology Fellowship at UCSF at the Early Phase Clinical Trials Unit. She published more than 20 papers in high impact peer reviewed journals in the areas of pediatric dosing guidelines, pediatric pharmacokinetic-outcome associations and biomarkers of response. pediatric board trainer since 2011.