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

Cancer drug resistance is a consequence of a complex, multidimensional interplay between tumor, its environment and the host. Drugs are often assumed to distribute relatively homogeneously from plasma to tumor tissues. However, distribution of drug in tumors is highly variable and may not correlate with dose or plasma concentrations. Solid tumors are characterized by a complex and unique microenvironment that consists of infiltrating immune cells, low pH, dense interstitial matrix, high interstitial pressure, and abnormal blood and lymphatic vascular structures. Overexpression of drug efflux transporters such as P-glycoprotein (MDR1/ABCB1), breast cancer resistance protein (BCRP/ABCG2), and transporters of the multidrug resistance-associated protein subfamily (MRP/ABCC) may also limit drug penetration in cancer cells or other (off) target cells. Variability in these factors among cancer types may be a contributing factor why translation from adults to pediatric patients often fails.

Until recently, assessment of spatial drug distribution in cancer cells or other target cells and clinical implementation of these data was limited by technical challenges. New technologies such as mass spectrometric and radiolabeled drug imaging address these challenges and illustrate the promise of applying imaging for optimal development and precision dosing and can be directly applied in pediatric dosing studies. In the presentation we will present an overview of our current knowledge of the association between drug penetration in plasma and target (cancer) cells and their effect on tumor response and discuss approaches for performing measurements of drug uptake at the pharmacological target site in pediatric patients.

Biography

Imke H Bartelink completed her PharmD and PhD from the Utrecht Medical Center in Utrecht, the Netherlands and Post-doctoral studies in Integrative Pharmacology from the University of California, San Francisco (UCSF). Currently, she has Clinical Pharmacology Fellowship at UCSF. She published more than 20 papers in high impact peer reviewed journals in the areas of pharmacokinetics, pharmacodynamics and biomarkers of response.

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