CONCLUSIONS: HPV vaccination may substantially reduce the clinical vulnerabilities in real-world settings, even when vaccination is incomplete. Policy and clinical efforts for HPV vaccination should focus on encouraging eligible girls to initiate vaccination.

PCN17 PREDICTING PHASE III SURVIVAL OUTCOMES USING PHASE II TRIAL DATA IN NSCLC AND RCC

OBJECTIVES: Over 50% of oncology drugs fail in Phase III clinical trials. It remains imperative to better define ways of predicting whether a drug will demonstrate clinical activity in Phase III trials before embarking on Phase III clinical trials. This research aims to explore whether Overall Response Rates (ORRs) from Phase II trials can predict the success of Phase III trials.

METHODS: Phase III data of any Non-Small Cell Lung Cancer (NSCLC) and Renal Cell Carcinoma (RCC) oncologic appraised by the FDA, or that had failed Phase III clinical trials, since 2002 was extracted along with its corresponding Phase II data. 28 oncologies were identified with both Phase II and III readouts (NSCLC: 18, RCC: 10) only 12 (43%) of which met their Phase III trial endpoint. We determined the number of Phase II ORRs > 0% and ≤ 61% and compared, on average, to those seen in their corresponding Phase III trials (95%). 7/10 (70%) drugs with Phase II ORRs > 30% met their primary endpoint vs. only 5/18 (28%) with ORRs ≤ 30%. This threshold is dependent on whether the Phase III trial is active or placebo-controlled. For active-controlled Phase III trials, 3/4 (75%) met their primary endpoint with Phase II ORRs > 30% vs. 5/18 (28%) with ORRs ≤ 30%. For placebo-controlled Phase II ORRs > 16% versus only ≤ 9/9 with ORRs ≤ 16%. CONCLUSIONS: The magnitude of ORRs seen in Phase II can be correlated with later Phase III trial success in NSCLC and RCC. A higher Phase II ORR threshold applies where comparative benefits need to be shown over an active comparator in Phase III versus only 5/18 (28%) with ORRs ≤ 30%. Further research can better define such thresholds apply to other tumor types and whether this threshold can predict future Phase III trial failures and successes.

PCN18 URSEDOXYCHOLIC AND CHENODEOXYCHOLIC ACID EXERT DISTINCT CYTOTOXIC EFFECTS ON COLON CANCER CELLS

OBJECTIVES: Hydrophobicity is the most important determinant of toxicity of bile acids (BAs) and depends on the number, position and orientation of hydroxy groups. Ursodeoxycholic acid (UDCA) is a hydrophilic dihydroxy BA, which is formed by β-oxidation of chenodeoxycholic acid (CDCA). The latter is a hydrophobic BA. Unlike the other secondary BAs, UDCA exerts antiapoptotic effects by oxidative stress. The aim of our study was to analyze the influence of stereochi-metry in BA activity on the cytotoxicity of UDCA and CDCA on colorectal adenocarcinoma HT-29 cells were used to assess the cytotoxicity of CDCA and UDCA using colorimetric MTT assay. In order to obtain explained results of MTT assay, 12, 24 and 48 hour period of treatments were included. The IC50 values were calculated from 3D structures of CDCA and UDCA using VolaSurf software. RESULTS: Studied BAs displayed distinct degrees of cytotoxicity towards HT-29 cancer cells in a concentration-dependent manner. Concentrations of CDCA and UDCA that inhibited cell viability by 50% (IC50) were 19.6 μM and 351 μM, respectively. Oxidative stress is considered to be the most plausible mechanism of cytotoxicity of BAs, which is determined mostly by their hydrophobicity. Calculated molecular descriptor that may explain these distinct cytotoxic effects is amphiphilic moment (A), which is defined as a vector pointing from the centre of hydrophilic domain to the centre of hydrophobic domain. The vector length (5.62 of CDCA and 4.87 of UDCA) determines the ability of compound to permeate a membrane. This was additionally substantiated with the values of Caco, skin and LgBB descriptors that indicate higher Caco-2 permeability, skin permeability and blood-brain barrier distribution of CDCA in comparison to UDCA. CONCLUSIONS: More pronounced antiapoptotic activity of CDCA in comparison to UDCA was observed. These data suggest that comparing the physicochemical properties of molecules may help in prediction of their cytotoxicity.