MOLECULAR CANCER THERAPEUTICS

HIGHLIGHTS

Selected Articles from This Issue

ASN004-5T4-targeting ADC with High Drug-to-antibody Ratio

Smith et al. | Page 1327

In this First Disclosure, Smith and colleagues describe ASN004, a Dolaflexin-containing antibody drug conjugate targeting the 5T4 oncofetal antigen expressed on a wide range of tumors. ASN004 contains a scFv-Fc antibody and a Auristatin F Hydroxypropylamide payload with a drug-to-antibody ratio of 10-12. In a single dose study, 1 mg/kg achieved complete tumor regression in a cervical cancer model. ASN004 was also shown to have greater activity than the HER2-targeted trastuzumab-DM1 in a gastric model with high HER2 expression despite low 5T4 expression. Pharmacokinetics revealed low free payload drug and dose-dependent exposure. Their results support the continued clinical development of ASN004.

Diabodies Targeting the hERG1/β1 Molecular Complex

Duranti et al. | Page 1338

In this First Disclosure, Duranti and colleagues outline a single-chain diabody targeting the hERG1 potassium channel and the β1 subunit of integrin receptors (scDb-hERG1-β1). The diabody bound with high affinity to the two proteins only when they were linked together and spared normal cells. The scDb-hERG1-β1 was antiproliferative against tumor spheroids through inhibition of AKT and HIF-1α signaling. The diabody also showed a favorable pharmacokinetic and toxicologic profile when injected into mice. Taken together, the disclosure provides evidence for the continued clinical development of scDb-hERG1-β1.

Gene Signature Correlates with Outcomes for Metastatic RCC

Yang et al. | Page 1454

VEGF inhibitors and immune therapies have continued to create favorable outcomes for renal cell carcinoma (RCC) patients. For those who don’t respond to these therapy options, Yang and colleagues hypothesized mTOR inhibition will remain a salvage option either by itself or in combined therapy. A recent clinical trial demonstrated mTOR inhibition combined with the vascular agent BNC105P failed to show increased efficacy compared to mTOR inhibition alone. In this study, they demonstrate the transcriptomic gene signatures of patients from that clinical study that correlated with benefit with mTOR inhibition. Their findings were then validated using the phase III CheckMate 025 study.

Consensus on Pediatric Preclinical Testing

Vassal et al. | Page 1462

There remains an urgent need for new drug discovery in pediatric cancer with an added goal of reducing long-term toxicity. In this article, Vassal and colleagues underline the outcome of a pediatric cancer international multistakeholder meeting to develop a consensus set of requirements for preclinical drug development in pediatric cancers. The recommendations include the use of cell-based and mouse models as well as proof-of-concept data packages for clinical development. They are designed to represent the minimum guidelines necessary for the international development of drugs for pediatric cancer within the new regulatory environment set up by the RACE act.
Molecular Cancer Therapeutics

Selected Articles from This Issue

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