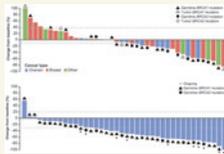


## Rucaparib in Germline *BRCA1/2*-mutated Ovarian Carcinoma

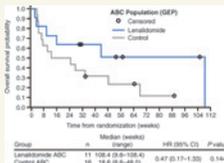


Defects in homologous recombination repair genes (e.g., *BRCA1* and *BRCA2* mutations) can sensitize tumors to poly (ADP-ribose) polymerase (PARP) inhibition through synthetic lethality. This phase I–II study was the first to evaluate single-agent oral rucaparib, a potent PARP inhibitor, at multiple doses in patients with advanced

solid tumors (Part 1; phase I), establish the recommended phase II dose (RP2D) of 600 mg twice daily, and evaluate the RP2D in patients with platinum-sensitive, high-grade ovarian carcinoma (HGOC) associated with a germline *BRCA1/2* mutation (Part 2A; phase II). Rucaparib was tolerable and had robust antitumor activity in patients with platinum-sensitive germline *BRCA1/2*-mutated HGOC. ■

See article by Kristeleit et al., p. 4095

## Lenalidomide Versus Investigator's Choice in DLBCL

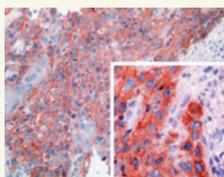


Germinal center B-cell (GCB) has a better prognosis than non-GCB diffuse large B-cell lymphoma (DLBCL) to upfront therapy. Cell-of-origin (COO) determination using gene expression profiling (GEP) is more sensitive, reproducible, and robust than immunohistochemistry. Czuczman and colleagues designed a randomized study using COO-based subtyping to elucidate differences in activity of

lenalidomide over salvage monotherapy in relapsed/refractory DLBCL. Lenalidomide elicited higher ORR and longer PFS in non-GCB patients (most pronounced in ABC-designated patients). These results provide an additional rationale for the ongoing phase 3 trial, ROBUST (NCT02285062), of lenalidomide plus immunochemotherapy versus immunochemotherapy alone in patients with treatment-naïve GEP-selected ABC-subtype DLBCL. ■

See article by Czuczman et al., p. 4127

## Identification of an $ITG\alpha_v\beta_6$ -Binding Peptide

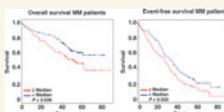


The improvement of imaging and therapeutic targeting of tumors requires the identification of novel target-specific tracers. To address HNSCC tumors, Altmann and colleagues performed alternating biopanning on membrane proteome of HNO97 tumor cells fractionated by the ProteomeLab PF2D system and corresponding HNO97 cells using a

sunflower trypsin inhibitor1-based phage display (SFTI8Ph) library. A novel  $ITG\alpha_v\beta_6$ -binding peptide (SFTIGv6) was identified providing high stability and demonstrating affinity for  $ITG\alpha_v\beta_6$ -positive HNSCC and other carcinomas. SFTIGv6 accumulated in tumor tissues but not in normal tissues or inflammatory lesions, and thus represents a promising tracer for imaging and endoradiotherapy. ■

See article by Altmann et al., p. 4170

## Targeting USP1 as Myeloma Therapy



Deubiquitylating (DUB) enzymes have emerged as potential therapeutic targets. Das and colleagues examined the functional significance of DUB enzyme USP1 in multiple myeloma (MM) using an irreversible USP1 inhibitor SJB3-019A. USP1 is highly expressed in patient multiple myeloma (MM) cells. USP1 blockade with SJB3-019A decreases the viability

of MM cells, inhibits DNA repair and USP1/ID/Notch/Sox pathways, and overcomes bortezomib-resistance. SJB induced generation of more mature and differentiated plasma cells. Combination of SJB with bortezomib, ACY1215, lenalidomide, or pomalidomide triggers synergistic anti-MM activity. These preclinical data provide basis for clinical evaluation of USP1 inhibitors in MM to overcome proteasome inhibitor resistance. ■

See article by Das et al., p. 4280

# Clinical Cancer Research

## Highlights of This Issue

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