had at least one line of systemic chemotherapy. Patients received RC48-ADC at 1.5 or 2 mg/kg, every two weeks. Clinical efficacy and safety were assessed.

Results: This study enrolled HER2-expressing metastatic SDC patients from June 2022 to Dec 2022. 10 mSDC patients (8 males, 2 females) were enrolled. 90% patients had received ≥2 lines systemic chemotherapy. 80% patients had visceral metastases. As of 05 Jan 2023 (data cutoff), 1 patient achieved CR, 4 patients achieved PR, 4 patients achieved SD, and only 1 patient achieved PD. The overall confirmed DCR was 90%. Most common treatment-related AEs were hypoaesthesia (70%), asthenia (60%), leukopenia (30%), decreased appetite (20%), alopecia (10%). The grade≥3 TRAEs only included hypoaesthesia (30.0%) and neutropenia (10%).

Conclusions: RC48-ADC showed a promising efficacy with a manageable safety profile in HER2-expressing mSDC patients who had failed at least one line of systemic chemotherapy.

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7P Global ring study determining reproducibility & comparability of CLDN18 testing assays in gastric cancer

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Background: Claudin-18.2 (CLDN18.2) the dominant isoform of CLDN18 in gastric tissue is a highly specific tight junction protein of the gastric mucosa expressed in gastric cancer & has emerged as a promising drug target. Zolbetuximab, a monoclonal antibody (Ab) targeting CLDN18.2 is reported to improve progression free & overall survival in combination with chemotherapy in the first-line treatment of CLDN18.2-positive, HER2-negative, locally advanced unresectable or metastatic gastric (G) & gastroesophageal junction (GEJ) cancers in 2 randomized phase 3 studies. Both studies (SPOTLIGHT, GLOW) met their primary endpoints. Patient selection for CLDN18.2 in these studies used the Ventana CLDN18 (43-14A) assay. It is important in the clinical setting to ensure accurate & reproducible results in the diagnosis of G/GEJ cancer for treatment options. This global ring study was conducted to assess analytical reproducibility & concordance of this assay with 2 other CLDN18 Abs (LSBio LS−B16145-100 & Novus Biologicals NBP2-32002) stained on 3 platforms to confirm possible diagnostic testing methods.

Methods: Tissue microarray (TMA) of 15 gastric cancer samples in triplicate cores was provided to 27 labs across 11 countries. Each lab stained the TMAs using 2-3 CLDN18 Abs with optimized protocols. The TMAs, also stained by the central lab, were used to achieve consensus by expert review. Using agreed scoring algorithms as per the phase 3 studies, IHC scores were generated per core & the results were collated for statistical analysis with the consensus results.

Results: Show high concordance among the 3 Abs across the assessed parameters when performed on each of the 3 platforms, with the highest accuracy & sensitivity observed for Ventana Ab & LSBio Ab across all 3 platforms.

Conclusions: The study shows multiple Abs applied on multiple platforms give highly reproducible and comparable results for detecting CLDN18.2 in gastric cancer providing a potential for their global adoption for CLDN18 testing.

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8P Targeting antiapoptotic Bcl-2 proteins with highly specific BH3 mimetics in solid tumors

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Background: Evasion of apoptosis is a hallmark of cancer survival and a reason for acquired resistance towards standard treatment, making it one of the challenges in modern cancer therapy. The antiapoptotic proteins Bcl-2, Bcl-x_L and Mcl-1, might be key to break such a resistance. In this study we evaluated the effects of highly specific inhibitors for Bcl-x_L (WEHI-539), Bcl-2 (ABT-199), and Mcl-1 (S63845) as well as dual inhibition of Bcl-x_L/Bcl-2 (ABT-263) in commonly occurring solid tumors.

Methods: Non-Small Cell Lung Cancer (NSCLC), Cholangiocarcinoma (CCA) and Breast Cancer cell lines were either exposed to fractionated photon radiation or chemotherapeutics (Epirubicin) as standard therapy with or without specific Bcl-2 protein inhibition. Protein expression was assessed via Western blots of cell lines. Effects on cell death were detected by flow cytometry measuring apoptosis.

Results: Dual Bcl-x_L/Bcl-2 inhibition led to significantly higher cell death induction in combination with radiotherapy in NSCLC and with Epirubicin in triple-negative breast cancer. Sole inhibition of Bcl-x_L caused an inferior but notable sensitization in both entities for standard therapy. In CCA, combination of fractionated photon beam radiation and specific Bcl-x_L inhibition showed a significant increase of cell death in all four employed cell lines. In addition, the triple-negative breast cancer cell line benefited synergistically from combined therapy with Mcl-1 inhibition and Epirubicin. In NSCLC, no correlation between basal expression of Bcl-2 family proteins and response to therapy was found and proteins were not regulated upon irradiation. Upregulation of Mcl-1 may play a role in promoting radioresistance after specific Bcl-2 and Mcl-1 inhibition. Following Epirubicin treatment, breast cancer cell lines showed a downregulation of antiapoptotic Bcl-2 protein expressions.

Conclusions: Our findings indicate that among antiapoptotic Bcl-2 proteins, targeting Bcl-x_L might break resistance to radiation in NSCLC, CCA and breast cancer in vitro. Especially for breast cancer, Mcl-1 could also be a promising target that needs to be further investigated.

Legal entity responsible for the study: The authors.

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9P An in vivo model for therapeutic antibody efficacy evaluation: The chicken embryo's CAM-based assay

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Background: Since its introduction, xenografts on the chicken embryo's ChorioAllantoic Membrane (CAM) has been proven extremely valuable for in vivo studies in cancerology. It is suitable to study tumor development, angiogenesis, malignant cell

Table: 7P

	Precision	Precision	Precision	Accuracy	Accuracy	Accuracy	Sensitivity	Sensitivity	Sensitivity	Specificity	Specificity	Specificity
Antibody	Ventana	Novus	LSBio	Ventana	Novus	LSBio	Ventana	Novus	LSBio	Ventana	Novus	LSBio
Platform												
Ventana	0.96	0.88	0.94	0.95	0.88	0.88	0.93	0.67	0.85	0.97	0.96	0.92
Dako	-	0.94	0.93	-	0.83	0.94	-	0.72	0.96	-	0.95	0.93
Leica	-	0.79	0.97	-	0.94	0.93	-	0.89	0.91	-	0.95	0.96