PET/CT IMAGING OF 64CU-LABELLED HER2 LIPOSOMAL DOXORUBICIN (64CU-MM-302) QUANTIFIES VARIABILITY OF LIPOSOMAL DRUG DELIVERY TO DIVERSE TUMOR LESIONS IN HER2-POSITIVE BREAST CANCER PATIENTS

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Introduction: MM-302 is a novel antibody-drug-conjugated (ADC) HER2-targeted PEGylated liposomal doxorubicin that specifically targets tumor cells overexpressing HER2 with minimal uptake into normal cells such as cardiomyocytes. We recently announced results from an ongoing Phase 1 clinical trial of MM-302 in HER2-positive metastatic breast cancer (NCT01304797), reporting that in patients treated with MM-302 monotherapy (n = 27), overall response rate was 15% (1 CR and 3 PRs) and estimated median progression free survival (PFS) was 5.6 months. Benefit was greatest in anthracycline-naive patients, of whom 4 of 9 achieved a response and 5 of 9 had PFS greater than 9 months. We have hypothesized that MM-302 delivery to tumors is variable and the extent of delivery may predict the probability of response to liposomal anti-cancer therapies. In the ongoing Phase 1 clinical trial, MM-302 was labeled with 64Cu (64Cu-MM-302) to enable study of its biodistribution and tumor accumulation in over 11 patients.

Materials and methods: 64Cu-MM-302 was prepared by a commercial radiopharmacy using 64Cu obtained from Washington University (St. Louis, MO USA). Patients received 30 mg/m2 of MM-302 followed by 400 MBq (10.8 mCi) of 64Cu-MM-302 (approx. 3-5 mg/m2 doxorubicin). PET/CT images were acquired 0–3 h after administration of 64Cu-MM-302 (day 1) and then on day 2 or day 3, or both. Late-time images were analyzed first to identify 64Cu-MM-302-avid foci. RECIST lesions from previous diagnostic CT images were then used to identify additional tumor lesions with low tracer uptake. Radiation dosimetry was estimated using standard methods and OLINDA.

Results: Uptake of 64Cu-MM-302 in tumor lesions increased over time relative to background. Median tumor activity ranged from 0.7 to 13.5 %ID/kg (n = 41 lesions) at 24 hours and from 0.5 to 17.7 %ID/kg at 48 hours (n = 25 lesions). 64Cu-MM-302-PET showed avid uptake in a brain metastasis and in bone lesions. The preliminary radiation dosimetry estimates were acceptable.

Conclusions: Preliminary results indicate that 64Cu-MM-302 can be used effectively to evaluate the biodistribution and tumor deposition of MM-302 in patients. Clinical biodistribution data were well predicted by preclinical models. Efforts to relate 64Cu-MM-302 tumor deposition to individual lesion response are ongoing.

Disclosure: B. Hendriks and T. Wickham: Employed by and holds stock and/or stock options in Merrimack Pharmaceuticals. A. Shields consults for Merrimack and ICON Medical Imaging relating to MM-302 and MM-DX-929, as well as receives funding for academic collaboration and clinical trial conduct at Karmanos Cancer Institute. B.A. Siegel consults for Merrimack and ICON Medical Imaging relating to MM-302 and MM-DX-929, as well as receiving funding for conduct MM-302 clinical trial at Washington University. K. Campbell and V. Moyo: Employed by and holds stock or stock options in Merrimack Pharmaceuticals. K. Miller, P. Munster, C. Ma and P. LoRusso: Receive funding to conduct MM-302 clinical trials from Merrimack Pharmaceuticals.

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