THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

Joseph A. Ludwig, MD

Associate Professor
jaludwig@mdanderson.org
T 713-792-3626 F 713-794-1934
Sarcoma Medical Oncology
1515 Holcombe Blvd.
Houston, TX 77030

Dear Mr. and Mrs. Tashman,

I want to express my sincere thanks and gratitude to you, your family and friends for your most generous donations to the research of desmoplastic small round cell tumor (DSRCT) in memory of Brett Tashman. Though I never had the opportunity to meet your son, the support that you, your family, and your many donors have provided our DSRCT research team is truly remarkable.

From the clinical perspective, in close collaboration with Dr. Andrea Hayes-Jordan over the last half decade, my team and I have helped formulate a treatment strategy used nationwide to help young DSRCT patients like Brett, who faced a difficult cancer battle. Our research demonstrates that chemotherapy and complete surgical cytoreductive surgery (CCS), of the type that Andrea is talented enough to perform, provides the greatest clinical benefit. Heated intraperitoneal chemotherapy and whole abdominal radiation are less commonly used today since our analysis indicated these modalities fail to meaningfully improve survival.

With respect to laboratory research, your generous philanthropy has aided in the development of a human patient-derived tumor explant (PDXs) panel, essentially a collection of mice bearing DSRCTs that had been extracted from patients and coaxed to survive and grow in animals. These PDXs are invaluable for drug discovery, as they allow our team to rapidly screen 6-10 drugs per year as a prelude to testing the most effective ones in early-phase human clinical trials.

Toward that end, we used the DSRCT PDX panel to identify two potent anti-cancer drug candidates that effectively kill DSRCT tumor cells. The first drug candidate takes aim at the EWSR1-WT1 fusion protein, the root cause of DSRCT responsible for tumor formation and growth. The second drug candidate targets the androgen receptor (AR), which is heavily expressed in prostate cancer and DSRCT. As shown in Figure 1, the EWSR1- and AR-targeted drugs significantly delay growth of DSRCT in our animal models compared to the placebo-treated mice. When combined, joint targeting of EWSR1 and AR led to even better results (red-colored line).

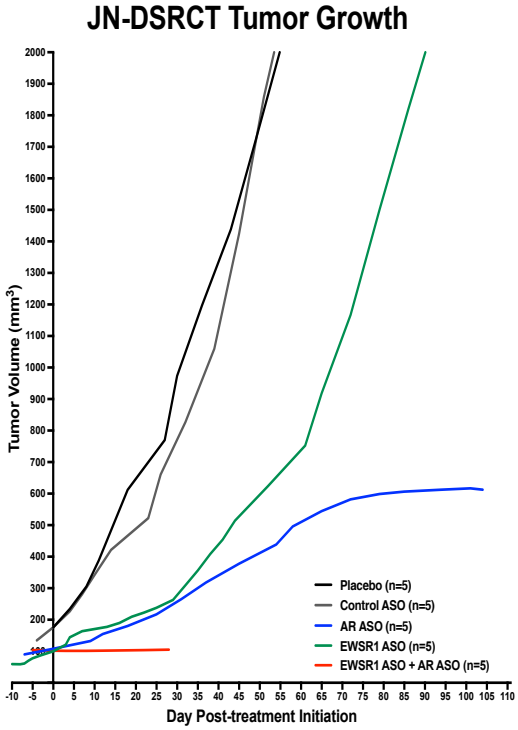

Figure 1. Evaluation of EWSR1- and AR-targeted therapies in DSRCT animal models.

Based upon the strength of these research findings, the FDA granted us permission to test AR-targeted therapies in a limited number of DSRCT patients under a compassionate access program (CIND; similar to right-to-try law), and a subsequent phase 2 trial is in development. On behalf of Andrea, and our entire research team, I thank you so much for your generous donations, which have been instrumental in our lab's mission to eradicate DSRCT. With 2019 right around the corner, I look forward to continuing our highly productive partnership and expect great clinical advancements.

Sincerely,

Joseph Ludwig, MD