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Original article

# Survival and toxicity following sequential multimodality treatment including whole abdominopelvic radiotherapy for patients with desmoplastic small round cell tumor

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ABSTRACT

*Background and purpose:* Desmoplastic small round cell tumor (DSRCT) is a rare, aggressive malignancy. We report survival rates and toxicity associated with sequential multimodality treatment including whole abdominopelvic radiation therapy (WART).

*Material and methods:* Medical records of 32 patients with DSRCT treated at our institution were reviewed. Patients underwent chemotherapy, cytoreductive surgery with hyperthermic intraperitoneal chemoperfusion (HIPEC), followed by WART with intensity-modulated radiation or volumetric-modulated arc therapy.

*Results:* Median overall survival (OS) was 60 months. After 18 months of follow-up, 20 patients (62.5%) had disease recurrence and median disease-free survival (DFS) was 10 months. Median time to extrahepatic abdominal failure was 19.4 months. Factors affecting time to local progression included liver metastases at diagnosis, and an interval of greater than 5.6 months between diagnosis and HIPEC or greater than 2.1 months between HIPEC and WART. None of these factors altered OS. Grade 3 or higher toxicities occurred in 84% of patients.

*Conclusions:* WART following chemotherapy, surgical cytoreduction and HIPEC is an aggressive treatment for DSRCT patients and can result in severe side effects. Our median OS of 5 years is favorable compared to prior studies, despite a median DFS of only 10 months, which may be due to improved salvage therapies.



DSRCT is a sarcomatoid malignancy that typically affects adolescent males and has a poor prognosis with median survival of only 17–25 months [1]. Most patients present with large intra-abdominal or pelvic masses; diffuse peritoneal metastasis (sarcomatosis) is common at the time of diagnosis. Currently, the standard treatment is induction chemotherapy with a Ewings-type regimen followed by surgical debulking [2]. More extensive surgical resection is associated with improved survival [3]; however, given intraperitoneal spread, while gross total resection is achievable, microscopic residual disease is expected.

To target microscopic residual disease, consolidative regimens including HIPEC and WART have been investigated. Surgical series from MD Anderson show that the addition of HIPEC to cytoreductive surgery is safe in children and may be associated with improved local control and overall survival in DSRCT patients [4,5]. Adjuvant radiation targeting the entire peritoneal cavity has also been used to target microscopic disease in DSRCT. WART was traditionally delivered using a 2-field AP-PA technique, which caused substantial gastrointestinal and hematologic side effects [2,6]. More recently, the dosimetric advantages of IMRT allow more conformal radiation to be delivered, specifically targeting areas of residual disease while sparing normal tissues, and early investigations with this technology suggest favorable toxicity profiles [7,8].

HIPEC and WART are not currently standard treatments for DSRCT [9]. However, a recent analysis of 197 DSRCT patients from two major centers showed improved survival in patients treated with radiation and intraperitoneal chemotherapy [10]. To date, most series assessing survival outcomes in DSRCT have included fewer than 10 patients receiving both HIPEC and WART. In this study, we analyzed 32 patients with a pathologic diagnosis of DSRCT treated at our institution with sequential therapy including

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**Table 1**
Characteristics and treatment details of the 32 DSRCT patients treated with sequential multi-modality therapy.

| | N (%) |
|---|---|
| *Gender (M:F)* | |
| Male | 28 (88) |
| Female | 4 (12) |
| *Median age at Dx (y) (range)* | 17.8 (5.2–49.9) |
| *Race* | |
| Caucasian | 23 (72) |
| Hispanic | 7 (22) |
| Asian | 1 (3) |
| Middle-Eastern | 1 (3) |
| *Metastases at Dx* | 15 (47) |
| Extra-abdominal only | 6 (19) |
| Liver only | 2 (6) |
| Liver and extra-abdominal | 7 (22) |
| *Radiation* | |
| IMRT | 23 (72) |
| VMAT | 9 (28) |
| Boost to gross disease | 14 (44) |
| Completed treatment | 31 (97) |
| Treatment break | 1 (3) |
| Liver rind | 24 (75) |
| *Chemotherapy* | |
| Concurrent | 26 (81) |
| Adjuvant | 29 (91) |
| *Treatment duration (mo) (range)* | |
| Median time between diagnosis and surgery | 7.8 (3.7–29.4) |
| Median time between surgery and WART | 1.4 (0.7–6.1) |
| Median duration of radiation | 0.9 (0.7–1.2) |

neoadjuvant chemotherapy, cytoreductive surgery, HIPEC, and WART.

## Materials and methods

### *Patients*

After IRB approval, the charts of 32 patients with a pathologic diagnosis of DSRCT were reviewed. All patients were treated with multimodality therapy at MD Anderson Cancer Center from January 1, 2006 to March 1, 2014. Patients received neoadjuvant chemotherapy with the P6 regimen [2] or another Ewing-type regimen [11,12] (Supplementary Table 1). At the time of cytoreductive surgery and HIPEC, all patients had good performance status (Lansky play scale or Karnofsky performance score of 60 or higher) and a response to induction chemotherapy without active extra-abdominal metastases based on CT and/or PET-CT imaging. Cytoreductive surgery consisted of exploratory laparotomy and removal of tumor to less than 1 cm gross residual disease followed by HIPEC (intraperitoneal infusion of cisplatin 100 mg/m$^2$ heated to 40–41 °C over 90 min). Most patients (94%) had a gastrojejunostomy tube placed at surgery to facilitate enteral nutrition.

For WART, the entire peritoneal cavity comprised the clinical target volume (CTV). The CTV was treated to 30 Gy in twenty 1.5-Gy daily fractions. Nine patients were treated with VMAT and 23 patients were treated with IMRT. In 14 patients, areas felt to be at risk for residual disease were boosted to a total dose of 36–40 Gy using a simultaneous integrated boost. To minimize hepatic toxicity, the dose to non-peritoneal liver parenchyma was kept below 30 Gy in 24 patients, creating a "rind" of higher dose along the peritoneal surface (Supplementary Fig. 1). Normal tissue complication probability guidelines were used to limit dose to the liver with a goal of less than 1% chance of radiation-induced liver damage [13].

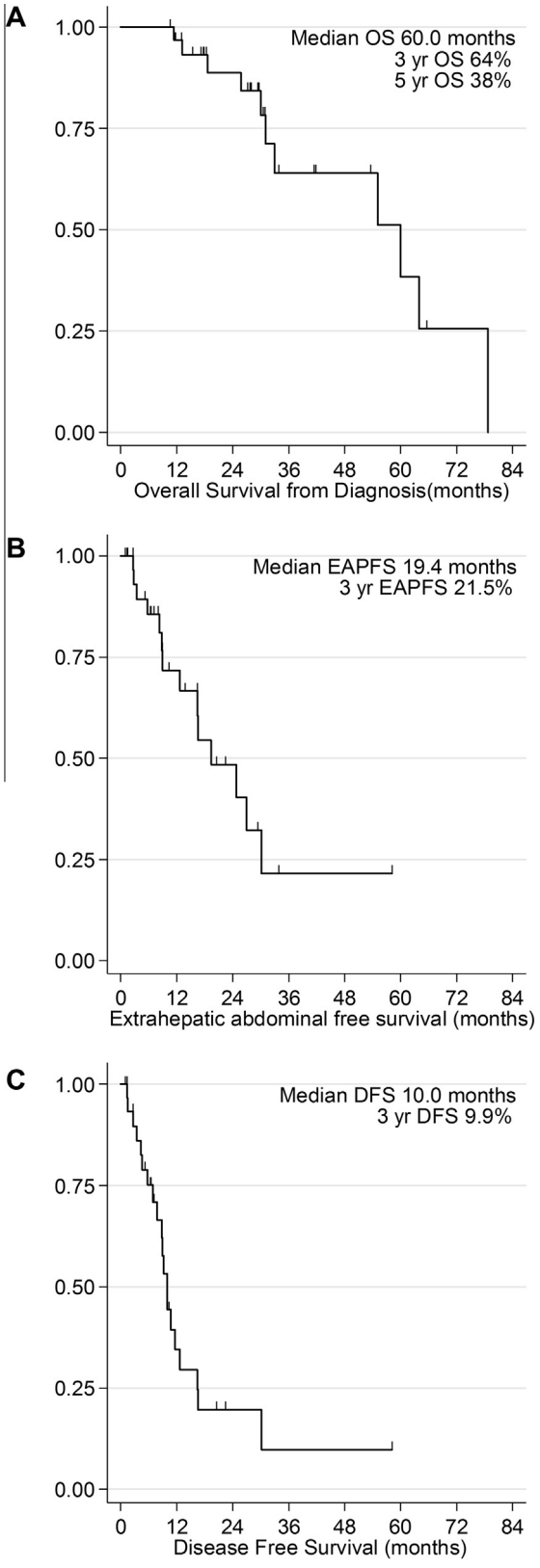


**Fig. 1.** Median survival after diagnosis of DSRCT in patients treated with sequential multi-modality therapy. (A) Overall survival (OS); (B) Extrahepatic intra-abdominal local progression free survival (EAPFS); (C) Disease free survival (DFS).

### *Toxicities*

Acute and late toxicities were graded according to CTCAE, version 4.0 [14]. Late toxicities were considered to be events occurring

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