Methotrexate Plus Vinorelbine (MTX/VBL) Chemotherapy for the Medical Management of Desmoid Fibromatosis (DF)

Gupta A[1,2], Burtenshaw SM[3], Thipphavong S[6], Byers N[2], Olteanu A[3], White L[6], Gladdy RA[3,4,5], Blackstein ME[2,5].

1 Department of Medical Oncology and Hematology, Princes Margaret Cancer Center, Toronto, ON, 2 Division of Medical Oncology and Hematology, Mount Sinai Hospital
3 Division of General Surgery, Mount Sinai Hospital 4 Department of Surgical Oncology, Princess Margaret Cancer Centre 5 Department of Surgery, University of Toronto, Toronto, ON,
6 Toronto Joint Department of Medical Imaging, University Health Network, Sinai Health System and Women's College Hospital, Toronto ON; Department of Medical Imaging, University of Toronto, Toronto ON

Objective

Desmoid Fibromatosis (DF) are locally aggressive benign neoplasms that can occur:

- sporadically
- in association with familial adenomatous polyposis (FAP)
- as a result of injury
- with a recent pregnancy[1]

Optimal management of these benign tumors remains controversial. Methotrexate plus Vinorelbine (MTX/VBL) is systemic therapy which is not associated with any long term sequelae. To date, reports of MTX/VBL have often included patients who have failed prior radiation therapy (RT) or other systemic therapy (ie. doxorubicin). We report our experience in management of patients with progressive DF with MTX/VBL, most of whom are treatment naïve.

Methods

Consecutive patients treated at Mount Sinai Hospital and Princess Margaret Cancer Centre with DF treated between Jan 1994 and Dec 2015 were reviewed.

Treatment: MTX 25 mg/m2 IV + VBL 25 mg/m2 IV d1,8,15 q28 d for a planned max duration of 24 cycles. Data including demographics, treatment details and toxicity were collected (Tables 1 and 2). A radiologist re-reviewed all available MRI scans to evaluate response by RECIST and T2 changes. PFS was estimated using KM and log rank statistical test.

Results

Table 1. Patient Demographics

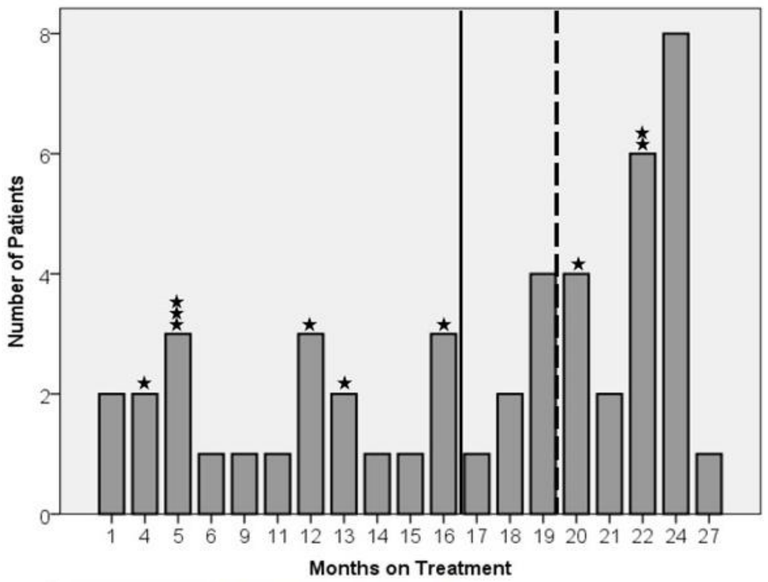
Number	**N=48**
Gender	**N (%)**
Female	31 (65)
Male	17 (35)
Age: median [range]	33 [13-73]
Location of DF	**N (%)**
Extremity	16 (33)
Abdominal wall	13 (27)
Head & neck	4 (8)
Chest wall/back	6 (13)
Mesenteric	7 (15)
Multifocal	2 (4)
Treatment naïve	37 (77)
Prior therapy	11 (23)
Surgery alone	6 (55)
Surgery and Tamoxifen	2 (18)
Surgery and RT	1 (9)
Tamoxifen alone	1 (9)
Tamoxifen and Doxorubicin	1 (9)

Table 2. Patient Response

Reasons for early therapy discontinuation before 24 mos	**N (%)** 39 (81)
Toxicity	2 (4)
Response achieved	28 (58)
Patient preference	8 (17)
Progressive disease	1 (2)
Toxicities	
Fatigue (grade 1/2)	9 (18)
Nausea	12 (25)
Fatigue & Nausea	4 (8)
Neutropenia (grade 1/2)	3 (6)
End of Therapy Response*	
Stable disease (SD)	8 (17)
Partial response (PR)	19 (40)
Complete response (CR)	20 (41)
Progressive disease (PD)	1 (2)

*Clinical benefit rate 98%

Figure 1. Months of Therapy and Recurrences in Patients with DF



★ = # of patients who progressed/recurred
┅ = median months on treatment
— = mean months on treatment

Median number of cycles of chemotherapy was 19 mos (range 1 to 27; Figure 1). Schedule modification occurred in 5 patients. The majority of patients (n=27, 56%) had 18 or more cycles of therapy; 9 completed 24 mos.

Figure 2. Five year PFS comparing length of treatment

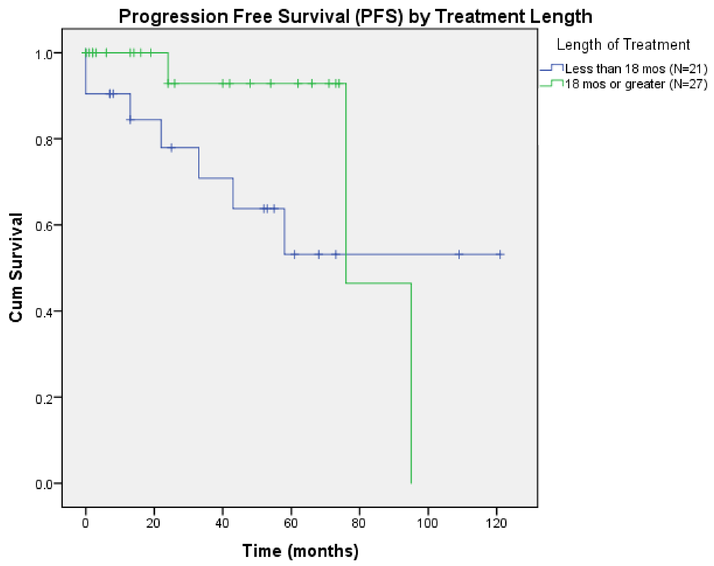


Figure 3. Pre-treatment MRI

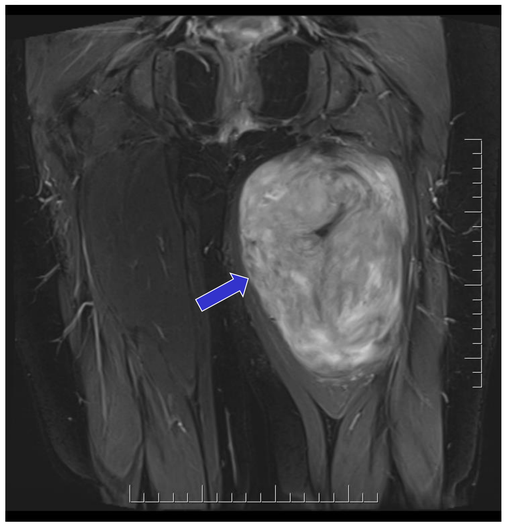
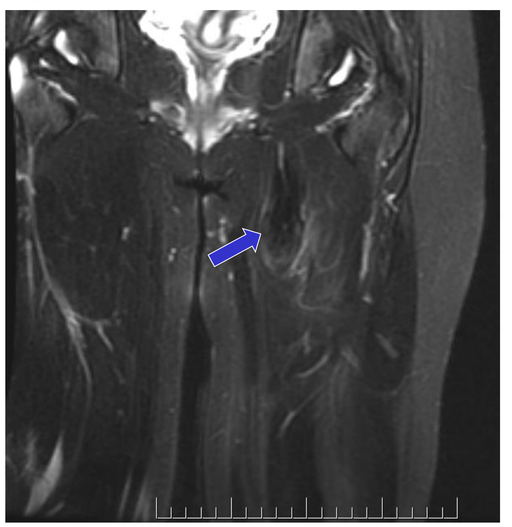


Figure 4. Post-treatment MRI (24 months)



Conclusion

MTX/VBL is very safe and very effective in the treatment of patients with DF and should be considered as first-line therapy. Duration of therapy of at least 18 months is likely required to ensure good outcome.

References:

1 Fletcher CDM, Bridge JA, Hogendoorn P., and Mertens F., eds. *WHO Classification of Tumours of Soft Tissue and Bone*. 4th ed. Lyon: International Agency For Research on Cancer, 2013.

We would like to express our thanks to the Wilson Sarcoma Research Fund for the continued support of the clinical research program at Mount Sinai Hospital/Princess Margaret Cancer Centre

Abstract: 2804802; Correspondence: Burtenshaw SM