# CTNNB1 MUTATIONAL STATUS DIRECTED TREATMENT MODALITY FOR PATIENTS WITH EXTRA-PERITONEAL DESMOIDS TUMORS

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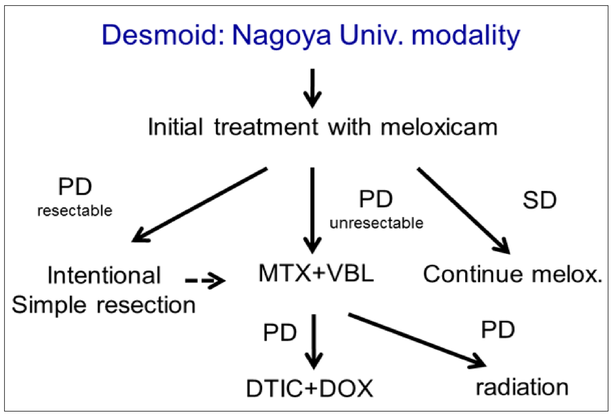
## INTRODUCTION

Extensive surgical resection has been the standard treatment for extra-peritoneal desmoid tumors decades. However, radical surgical intervention and/or repeated surgery due to a high recurrence rate [1], [2] occasionally lead to significant treatment-related morbidity.

The effectiveness of conservative treatment for desmoid tumors including radiotherapy and pharmacological treatment has been reported including anti-hormone, NSAIDs, and targeted and traditional cytotoxic chemotherapies [3–5]. However, the efficacy of these treatments cannot be predicted, and so remains a crucial problem.

## TREATMENT MODALITY in Nagoya Univ.

Since 2003, patients with extra-peritoneal desmoids tumors have been consecutively, prospectively treated with meloxicam, a COX-2 inhibitor, in our institutions. According to RECIST criteria, part of patients with SD and all patients with PD status were subjected to low-dose chemotherapy with MTX+VBL or planned simple resection based on the resectability or predicted functional impairment after surgery.

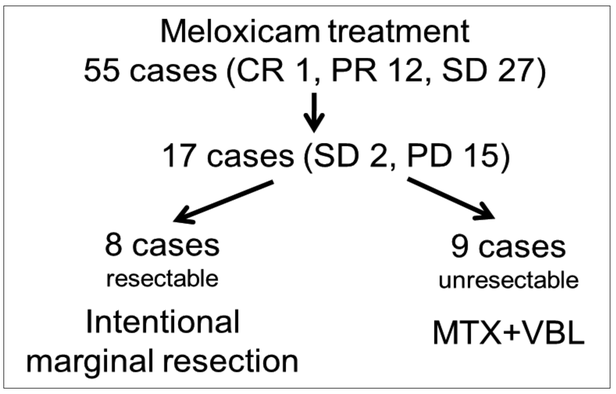


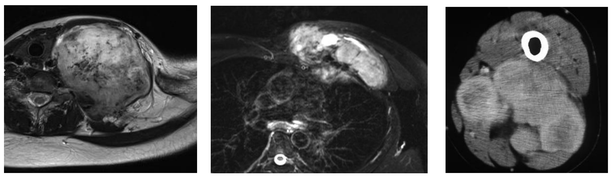

## OBJECTIVES

To clarify the usefulness of CTNNB1 mutational status to predict the efficacy of various therapeutic modality, Relationship between clinical outcome of various treatments and CTNNB1 mutational types were determined.

## METHODS

Since 2003, 55 patients were prospectively treated with meloxicam.



Biopsy specimens

CTNNB1 exon 3 sequencing

## RESULTS

(1) Among 55 patients prospectively treated with meloxicam, mutational status was determined in 33 cases.

Table 1. Relationship between efficacy of meloxicam and mutation type (33 cases)

| Variables | Mutation status WT (n=12) | T41A (n=16) | S45F (n=4) | S45P (n=1) | P value |
|---|---|---|---|---|---|
| Gender (Female/ Male) | 7/5 | 12/4 | 2/2 | 1/0 | 0.674 |
| Mean age, year | 45.0 | 40.7 | 38.5 | 26.0 | 0.574 |
| Mean Size, mm | 74.7 | 82.4 | 106.5 | 118.0 | 0.465 |
| Site | | | | | 0.230 |
| Abdominal wall | 4 | 1 | 1 | 1 | |
| Other trunk | 2 | 5 | 2 | 0 | |
| Neck | 1 | 3 | 1 | 0 | |
| Extremities | 5 | 7 | 0 | 0 | |
| Efficacy of meloxicam | | | | | **0.053** |
| Favorable group (CR,PR, SD) | 8 | 11 | 0 | 1 | |
| Unfavorable group (PD) | 4 | 5 | 4 | 0 | |

Table 2. S45F mutation status and efficacy of meloxicam

| | S45F (+) | S45F(-) |
|---|---|---|
| Favorable group (CR, PR, SD) | 0 | 20 |
| Unfavorable group (PD) | 4 | 9 |

P=0.017

(2) MTX+VBL treatment in 9 cases.

Table 3. Relationship between efficacy of MTX+VBL and mutation type (9 cases)

| | WT | T41A | S45F | S45P |
|---|---|---|---|---|
| Favorable (CR, PR, SD) | 1 | 2 | 4 | 1 |
| Unfavorable (PD) | 0 | 0 | 1 | 0 |

P=0.75

(3) Planned simple resection in 8 cases.
All cases were evaluated as margin positive.
Mean follow-up period was 37 months (16-58).

Table 4. Relationship between surgical outcome and mutation type (8 cases)

| | WT | T41A | S45F |
|---|---|---|---|
| No recurrence | 4 | 3 | 0 |
| Recurrence | 0 | 0 | 1 |

P=0.125

## DISCUSSION

A few studies have investigated the predictive value of catenin β-1 (CTNNB1) mutation for the outcome of surgical treatment. The results of these studies, however, have been controversial possibly because they focused on retrospective cohorts with inhomogeneous treatment [6-8].
The present study composed of identical cohort will provide possible predictive value of CTNNB1 mutation status for not only meloxicam treatment (conservative), but surgical treatment.
Although the current study is a pilot one based on small number of cases, accumulated number of cases will clarify the significance of CTNNB1 mutation status further.

## REFERENCES

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