Desmoïd Tumor Research Foundation (DTRF) annual meeting

Philadelphia, September 23 & 24, 2017

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D.J. Grünhagen, MD, PhD, surgeon, Erasmus MC
Introduction

Recurrence rates after treatment up to 69%\textsuperscript{11,15,16}

Wait & See policy for aggressive fibromatosis (AF)

Progressive disease < 2 yrs\textsuperscript{13,14,15}

Spontaneous regression 5-28% cases\textsuperscript{12,14}

Adverse treatment effects

Growth of aggressive fibromatosis without therapeutic intervention
**Start study:** May 2014

**Study design:** prospective observational study

**Study population:** patients diagnosed with aggressive fibromatosis (AF) with extra-abdominal or abdominal wall tumor localization
**Primary endpoint:** tumor progression (RECIST)

Progression = \( \geq 20\% \) of the sum of the **longest diameter**, in comparison with the **smallest sum of the longest diameter** since the time of inclusion.

**Secondary endpoint:** quality of life (QOL) during the W&S policy.
GRAFITI

Additional goals

Evaluate willingness of patients for a W&S policy

Analyze factors for the prediction of progression

Evaluate considerations for switch to active treatment
GRAFITI

Study goal: 100 patients

Inclusion rate: 62*
<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>extra-abdominal and abdominal wall AF</td>
<td>age &lt; 18 years</td>
</tr>
<tr>
<td>histologically proof of AF</td>
<td>medical / family history of FAP*</td>
</tr>
<tr>
<td>able to receive a MRI-scan</td>
<td>intra-abdominal tumor</td>
</tr>
<tr>
<td>No functional limitations due to the tumor</td>
<td>potentially life-threatening tumor</td>
</tr>
<tr>
<td>understand and sign informed consent</td>
<td>severe functional limitation in case of progression</td>
</tr>
<tr>
<td></td>
<td>unavoidable mutilation in case of progression</td>
</tr>
<tr>
<td></td>
<td>severe pain associated with the tumor</td>
</tr>
<tr>
<td></td>
<td>local or systemic therapy for the current manifestation of AF</td>
</tr>
</tbody>
</table>

*Familial adenomatous polyposis (FAP)
## Follow-up

<table>
<thead>
<tr>
<th></th>
<th>Inclusion</th>
<th>Year 1</th>
<th>Year 2</th>
<th>Year 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Months</strong></td>
<td>3</td>
<td>6</td>
<td>9</td>
<td>12</td>
</tr>
<tr>
<td>Medical history and physical examination</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>MRI-scan</td>
<td>x</td>
<td></td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>x</td>
<td>x</td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>EORTC qlcq-30 questionnaire</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td></td>
</tr>
</tbody>
</table>
Interim analysis

Inclusion of the **first 20 patients**, with **complete** 1 year follow-up

**Continuing the GRAFITI:**

> 50% has to have a W&S policy 1 year after inclusion
Patient characteristics I

15:5

median 12 weeks (range 1 - >104 weeks )

- extremity: 7 (35%)
- abdominal wall: 6 (30%)
- thorax: 4 (20%)
- head / neck: 1 (5%)
- back: 2 (10%)

- solitary lesion: 17 (85%)
- multiple lesions: 3 (15%)
## Patient characteristics II

<table>
<thead>
<tr>
<th>tumor growth</th>
<th>yes</th>
<th>11 (55%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no</td>
<td>8 (40%)</td>
</tr>
<tr>
<td></td>
<td>unknown</td>
<td>1 (5%)</td>
</tr>
</tbody>
</table>
Patient characteristics II

<table>
<thead>
<tr>
<th>Tumor growth</th>
<th>Yes</th>
<th>11 (55%)</th>
<th>0-2 cm / month</th>
<th>6 (55%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>8</td>
<td>(40%)</td>
<td>2-5 cm / month</td>
<td>1 (9%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>1</td>
<td>(5%)</td>
<td>Not specified</td>
<td>4 (36%)</td>
</tr>
</tbody>
</table>

Median size at palpation 3 cm (range 0-10 cm)
## Patient characteristics III

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Inclusion</th>
<th>3 M</th>
<th>6 M</th>
<th>9 M</th>
<th>12 M</th>
</tr>
</thead>
<tbody>
<tr>
<td>none</td>
<td>7 (35%)</td>
<td>9 (45%)</td>
<td>8 (40%)</td>
<td>5 (25%)</td>
<td>5 (25%)</td>
</tr>
<tr>
<td>sensory</td>
<td>6 (30%)</td>
<td>6 (30%)</td>
<td>3 (15%)</td>
<td>4 (20%)</td>
<td>7 (35%)</td>
</tr>
<tr>
<td>motoric</td>
<td>1 (5%)</td>
<td>1 (5%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>other**</td>
<td>5 (25%)</td>
<td>3 (15%)</td>
<td>2 (10%)</td>
<td>2 (10%)</td>
<td>0</td>
</tr>
<tr>
<td>unknown</td>
<td>1 (5%)</td>
<td>1 (5%)</td>
<td>2 (10%)</td>
<td>4 (20%)</td>
<td>0</td>
</tr>
</tbody>
</table>

**Visit Analogue Scale (VAS)**

1-4 mild pain
5-6 moderate pain
7-10 severe pain
unknown

<table>
<thead>
<tr>
<th>VAS*</th>
<th>Inclusion</th>
<th>3 M</th>
<th>6 M</th>
<th>9 M</th>
<th>12 M</th>
</tr>
</thead>
<tbody>
<tr>
<td>mild pain</td>
<td>14 (70%)</td>
<td>11 (55%)</td>
<td>8 (40%)</td>
<td>8 (40%)</td>
<td>7 (35%)</td>
</tr>
<tr>
<td>moderate pain</td>
<td>1 (5%)</td>
<td>1 (5%)</td>
<td>1 (5%)</td>
<td>1 (5%)</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>severe pain</td>
<td>0</td>
<td>2 (10%)</td>
<td>1 (5%)</td>
<td>1 (5%)</td>
<td>0</td>
</tr>
<tr>
<td>unknown</td>
<td>4 (20%)</td>
<td>6 (30%)</td>
<td>5 (25%)</td>
<td>5 (25%)</td>
<td>7 (35%)</td>
</tr>
</tbody>
</table>

* Heavy feeling, stabbing pain, pain at sports, pain at abdominal pressure, heavy menstruation, very minor pain, minor motoric limited function
Results

20 patients

15 (75%) W&S

5 (25%) Switch to active treatment

3 months after inclusion
Results

20 patients

15 (75%) W&S

3 months after inclusion

5 (25%) Switch to active treatment

Surgery N = 3

Radiotherapy N = 2
Results

20 patients

15 (75%) W&S

5 (25%) Switch to active treatment

3 months after inclusion

Surgery N = 3

Patient initiated N = 2

Specialist initiated N = 1

Radiotherapy N = 2

Patient initiated N = 1

Specialist initiated N = 1

↑ Symptoms

Growth
Results

- Progression: N = 1
- Regression: N = 0
- Stable disease: N = 8
- Unknown*: N = 6

20 patients

15 (75%) W&S

5 (25%) Switch to active treatment

3 months after inclusion

* No measurements available
Switch to active treatment

<table>
<thead>
<tr>
<th>sex</th>
<th>male</th>
<th>female</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>median age</th>
<th>22 years (19-33 years)</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>medical history of prior desmoid</th>
<th>no</th>
<th>yes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3</td>
<td>2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>localization</th>
<th>extremity</th>
<th>abdominal wall</th>
<th>back</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>surgery at tumor site</th>
<th>no</th>
<th>yes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>number of tumors</th>
<th>solitary</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5</td>
</tr>
</tbody>
</table>
Conclusion - I

> 50% of patients with AF continue a W&S policy in the GRAFITI study

It is **safe** to continue the GRAFITI study.
<table>
<thead>
<tr>
<th>QOL</th>
<th>functional scales</th>
<th>symptom scales</th>
<th>single items</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>physical functioning</td>
<td>fatigue</td>
<td>dyspnoea</td>
</tr>
<tr>
<td></td>
<td>role functioning</td>
<td>nausea and vomiting</td>
<td>insomnia</td>
</tr>
<tr>
<td></td>
<td>emotional functioning</td>
<td>pain</td>
<td>appetite loss</td>
</tr>
<tr>
<td></td>
<td>cognitive functioning</td>
<td></td>
<td>constipation</td>
</tr>
<tr>
<td></td>
<td>social functioning</td>
<td></td>
<td>diarrhoea</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>financial difficulties</td>
</tr>
</tbody>
</table>

Measured by EORTC QLQ-c30 questionnary
Quality of life

W&S

Switch to active treatment

Global health status (QoL)

Social function

Emotional function

Cognitive function

Physical function

Role function

* Data obtained from EORTC reference values manual
Quality of life

W&S

Switch to active treatment

* Data obtained from EORTC reference values manual
It is **safe** to continue the GRAFITI study.

QOL in the W&S group is comparable to the QOL measured in the general population.
Questions?

Thank you for your attention

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