Assessment of OMERACT Global Power Doppler Ultrasonography 44-Joint Scoring System and Reduced Joint Scoring Systems in Rheumatoid Arthritis Patients Treated with Abatacept Plus Background Methotrexate

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Bristol Global score = EF and IM: Bristol

Range: 0 (normal joint) to 3 (severe synovitis)

Combining grayscale synovial hypertrophy and Power Doppler

Total synovitis score = synovitis of an individual joint

Applicable to all joints and consistent between machines
e.g. for MCPs 2
No consensus on number of joints

This study was sponsored by Bristol

Elsevier (b

The OMERACT Ultrasound Task Force has worked

Ultrasound in RA sensitive to

Changes –

- Grayscale: signal = measure of blood flow or 'vascularity'
- Doppler: signal = measure of blood flow or 'vascularity'
- Semi-quantitative1 – Number of color pixels in ROI12
- Quantitative – Time–intensity curves (bubble contrast)1

Use of Ultrasonography to Detect Synovitis

Open Questions in Use of Ultrasound Assessments in RA

• Ultrasound in RA sensitive to change
  – Many differences in responsiveness index used (GS, Doppler or both?)
  – No consensus on number of joints

• Need to define
  – Minimum subset of joints to be examined to adequately monitor disease activity
  – Appropriate scoring system (joint level → patient level)

Disclosures

• This study was sponsored by Bristol-Myers Squibb
• Financial disclosure (MADA)
  – Bristol-Myers Squibb (consulting fees)
  – Roche, BMS, Pfizer, Abbott, UCB (speakers bureau)
  – PRHC (research grant)
  – Elsevier (book royalties)

• Disclosures for all co-authors are:
  – RW, HSÉ, OV, MG, PB, AI and EN: nothing to disclose
  – CG, KVH and MLB: Bristol-Myers Squibb (employees)
  – EF and IM: Bristol-Myers Squibb (consulting fees)
  – MD: Abbott, Bristol-Myers Squibb, Pfizer/Wyeth, Centocor/Jansen, Schering-Plough & MSD, Roche, UCB (research grants, consulting fees and/or speakers bureau)

Scoring Synovitis:

the OMERACT Ultrasound Task Force

• The OMERACT Ultrasound Task Force has worked towards development of a reliable, standardized global scoring system for synovitis in RA
  – Applicable to all joints and consistent between machines
  – Combining grayscale synovial hypertrophy and Power Doppler signal

• Total synovitis score = synovitis of an individual joint
  – Range: 0 (normal joint) to 3 (severe synovitis)

• Global score = sum of total synovitis scores
  – e.g. for MCPs 2–5: range 0–24

Responsiveness of PDUS

Phase IIb international study performed to evaluate the responsiveness of PDUS in RA and assess the early effect of abatacept + MTX on synovitis in affected MCP and non-MCP joints, using the global OMERACT-EULAR PDUS synovitis score

Exclusion Criteria

RA (lesser metacarpal diaphysis), MTP-IP and troclear axils, DMARD- or biologic active, visible synovitis score ≥ 3 at MTP-J or MTP-I and CRP ≥ 25 mg/L

Primary Endpoint

Global PDUS synovitis score (MTP 3–14)

Concomitant MTX

Follow-up: 16 weeks

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<thead>
<tr>
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<td>D1</td>
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n=104

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n=89
**Study Objectives**

- **Primary**
  - Assess early signs of response to ABA + MTX through PDUS assessment of MCPs 2–5
- **Exploratory**
  - Identify a minimum set of joints to be monitored to adequately assess disease activity

**Primary Endpoint (MCPs 2–5): Mean Change in Global PDUS Score Over 6 Months**

<table>
<thead>
<tr>
<th>Study visit day</th>
<th>Global PDUS (22-paired joint) score</th>
<th>Swollen joint count</th>
<th>Tender joint count</th>
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<tbody>
<tr>
<td></td>
<td>Mean baseline score (95% CI)</td>
<td>Day 7</td>
<td>Day 7</td>
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<tr>
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<td>39.4 (35.7, 43.0)</td>
<td>-1.7 (-3.4, -0.1)</td>
<td>-3.8 (-4.7, -2.9)</td>
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<td>Day 169</td>
<td>-15.7 (-19.0, -12.5)</td>
<td>-8.2 (-9.5, -6.8)</td>
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<tr>
<td></td>
<td>Mean change from baseline (95% CI)</td>
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<td>Change in Global PDUS (22-Paired Joints) Score, SJC and TJC over 6 Months</td>
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**Exploratory Analysis: Mean Change in Global PDUS (22-Paired Joints) Score Over 6 Months**

**Reduced Set of Joints: Methodology**

- Principal Component Analysis on 22 pairs of joints performed separately at baseline, D85 and D169
  - Subsets to explain at least 75% of the total variation based on Eigen values (of correlation matrix)
- Identification of 2 best subsets for each time point:
  - Using Joliffe methods B2 and B4 (deletion or addition)
- Selection of the optimal reduced set of joints among the different identified subsets:
  - Based on values of the efficiency measure (EM) of each reduced subset evaluated at 3 time points (baseline, D85 and D169)
  1) EM >0.6 at all 3 time points
  2) Subset with highest minimum EM over the 3 time points

**The Best Reduced Set**

- 9 paired joints
  - Shoulder, elbow, wrist, MCP1, MCP4, PIP2, knee, MTP3 and MTP5
This study confirms that PDUS is a sensitive tool. Further studies are needed to confirm the best reduced subset of joints to monitor disease activity at patient level.

Conclusions

- In patients with RA and MTX-IR, abatacept + MTX resulted in early and continuous signs of improvement in synovitis, as assessed by changes in Global PDUS score from Day 7 up to Day 169.
- Exploratory analysis suggest:
  - A reduced set of 9-paired joints that best represented the Global 22-paired PDUS score could be identified by PCA.
  - Similar kinetics of improvement with global PDUS 22-paired joint and 9-paired joint subset.
- This study confirms that PDUS is a sensitive tool.
- Further studies are needed to confirm the best reduced set of joints to monitor disease activity at patient level.

Acknowledgments (1): Principal Investigators
Acknowledgments (2)

- OMERACT-EULAR Task Force and Maarten Boers
- Statistical support was provided by Emilie Barré, Harry Goyvaerts, Wendy Kerselaers, Nathalie Schmidely (Bristol-Myers Squibb) and Coralie Poncet (Docs International)
- Editorial support was provided by MaiLee Wong, Caudex Medical, and was funded by Bristol-Myers Squibb
- CRO services were provided by Nabil Alt-oukhtar and Christel Peronne of ICON and was funded by Bristol-Myers Squibb