

**SUPPLEMENTARY MATERIALS****THE IMPACT TRIAL: INVESTIGATING METHOTREXATE POLYGLUTAMATE ASSESSMENTS IN COMBINATION THERAPY****DIFFERING CONTRIBUTION OF METHOTREXATE POLYGLUTAMATE TO ADALIMUMAB STEADY STATE LEVELS AS COMPARED TO ETANERCEPT**Thierry Dervieux<sup>1</sup>, Joel Kremer<sup>2</sup>, Michael Weinblatt<sup>3</sup><sup>1</sup>Exagen, Vista, CA; <sup>2</sup>The Center for Rheumatology, Albany, NY;<sup>3</sup>Brigham and Women Hospital, Boston, MA.**Supplementary Table I:** Patient demographics.

All patients enrolled received MTX in combination with anti-TNFs therapy for at least three months.

	MTX + Adalimumab	MTX + Etanercept
<b>Number of patients</b>	83	86
<b>Age (years)</b>	58±1	59±1
<b>Gender (% female)</b>	82%	86%
<b>Obese (BMI&gt;30 Kg/m<sup>2</sup>)</b>	37%	41%
<b>Disease duration (years)</b>	8±1	12±1
<b>Anti-TNF dose [mg/week]</b>	21±1	49±1
<b>Duration of TNF [months]</b>	83±4	86±5
<b>Previous anti-TNF [%]</b>	22%	12%
<b>Anti-TNF levels [µg/ml]</b>	11.8±0.8	3.2±0.2
<b>Undetectable anti-TNF blood levels<sup>1</sup></b>	3.6%	0.0%
<b>MTX dose [mg/week]</b>	16.7±0.7	16.4±0.6
<b>Duration of MTX [months]</b>	95±8	109±8
<b>Short chain MTXPG<sub>1-2</sub> [nmol/L]</b>	40±3	48±4
<b>Long chain MTXPG<sub>3</sub> [nmol/L]</b>	38±2	39±4
<b>Very long chain MTXPG<sub>4-5</sub> [nmol/L]</b>	14±2	14±2
<b>DAS 28</b>	2.8±0.2	2.7±0.2
<b>DAS 28 remission (DAS28&lt;2.6)</b>	43%	44%
<b>CRP [mg/dl]</b>	7.0±0.4	9.0±0.9

Results are expressed as mean [SEM], or percentage, as appropriate. Lower limit of quantification is 0.65 µg/ml for infliximab and adalimumab, and 0.1 µg/ml for etanercept.

**Supplementary Table II:** RBC short chain, long chain and very long chain MTXPG levels and steady state levels for adalimumab as compared to etanercept.

	MTX + Adalimumab	MTX + Etanercept
Short chain MTXPG <sub>1-2</sub>	0.042±0.029 (p=0.16)	0.004±0.007 (p=0.50)
Long chain MTXPG <sub>3</sub>	0.074±0.029 <sup>a</sup> (p=0.01)	-0.008±0.010 (p=0.44)
Very-long chain MTXPG <sub>4-5</sub>	0.071±0.036 (p=0.05)	-0.017±0.013 (p=0.22)

All estimates are adjusted for anti-TNF dosage (mg per week), CRP (mg/dl), obese status (BMI>30 Kg/m<sup>2</sup>), disease duration (years) and previous anti-TNFs treatment, as described in **Table I**. <sup>a</sup>Each unit in RBC MTXPG<sub>3</sub> (expressed as nmol/L) was associated with 0.07 units higher adalimumab levels (expressed as µg/ml). MTXPG: methotrexate polyglutamate.