Welcome to the Post Biologic Era

David Walker & Sandra Robinson
Perspective:

- 1978 SHO Gold & Penicillamine. Erosion pre-treatment
- 1984 SR 20% DMARD Sulphasalazine
- 1994 Cons 60% DMARD Methotrexate
- 2002 80% DMARD Leflunomide & TNFi & Rituximab
- 2012 90% DMARD Tocilizumab & Abatacept
- 2014 EAC

Waiting Time

- 13 weeks
- 13 weeks
- 18 weeks
- 52 weeks
- 12 weeks
- 2 weeks
Keeping the patient on board

- Here is a booklet on your diagnosis.
- And this is what a DAS score is.
- And: I want to start you on this drug...
- And this one....
- And this one....
- And this one....
- And this one....
- And: Healthcare at its very best - with a personal touch.
Treat to target

- Fashionable
- Works in studies but some tortology
- Difficult round the fringes: Are you really going to go for a biologic to get from 2.8 to 2.6?
- Negotiating the target: What would you like your DAS to be?
Tolerability/Adherence

- 56% to 85% of patients on a stable dose of Methotrexate are suffering from side effects.
- 51% would be attracted to a drug regime that did not include Methotrexate.
- Are they taking it?
- Most Nurses believe that patients would not be open about it.
- Most doctors don’t believe that.
Does tolerance have an impact on adherence?

- In 2011 we wondered if there should be a standard for Methotrexate Tolerance

- We asked 100 patients who had never reported side effects if they suffered any

- 56% said yes

- This audit was repeated in 6 centres across the UK

S Robinson; S Gibson; E George; U Martin; P Heslop; H Wrightson; P Prowse; M Kalinowski; D Marshall; M Reed; A Adebajo; D Walker. Tolerability and Adherence problems in patients on a stable dose of Methotrexate: Results of a multi-centre survey. Musculoskeletal Care 2015; 14,152-155.
Total Percentage of Any Side Effects
Chose or forgot to take

- Newcastle
- Barnsley
- Wirral
- Waterford
- Basingstoke
- Glasgow
- North Tyneside

Legend:
- Green: Chose
- Pink: Forgot
~70% of non-adherence is intentional\(^1\)

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Cognitive ability, depression, social support, coping skills</th>
<th>Concerns about treatment (fear of side effects etc)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Income</td>
<td>Number of medicines, disease seriousness beliefs</td>
<td>Beliefs about illness (cause, timeline)</td>
</tr>
<tr>
<td>Age</td>
<td>Health literacy, locus of control</td>
<td>Beliefs about cost of therapy</td>
</tr>
<tr>
<td>Race</td>
<td>Self-efficacy, trust in HCP, HCP-patient concordance</td>
<td>Necessity (perceived need) for treatment</td>
</tr>
<tr>
<td>Income, personality</td>
<td>Symptom experience</td>
<td>Perceived drug efficacy</td>
</tr>
</tbody>
</table>

Why do Patients not tell us?

- Do not want to disappoint
- Do not think there is anything else they can take
- Are managing their disease and side effects adequately
- To not want to appear to be “breaking the rules”
- Are afraid medication will be stopped
In 2002 MC, a self-employed painter and decorator aged 54, presented to his GP with joint pain, who prescribed Diclofenac. He also took Chinese Herbal Medicines. But by March 2003, his symptoms had worsened and he was referred to a Rheumatologist.

28/03/03 Referred to Rheumatologist, polyarthritis loss of joint movement diagnosis PsA.

29/08/03 MC reports no side effects, but does have wrist pain.

16/01/04 Seen by nurse, no problems.

Seen 6 monthly by Rheumatologist and Nurses, 16/01/04 – 08/02/08 has occasional wrist problems requiring joint injections. No side effects.

08/02/08 Wrists becoming more painful despite injections.

Continues 6 monthly appointments with Rheumatologist and Nurses, reporting no problems.

09/01/15 PsA remains under good control, admitted that has had nausea with MTX for years and has only taken half of the dose. Had deliberately not mentioned having side effects in the last 12 years.

MTX 10mg
What prompted the patient to reveal his partial adherence?

- The Health Care Professional had been chatting to the patient about side effects and revealed that an anaesthetist colleague did not adhere to treatment.

- This empowered the patient to reveal his partial adherence to treatment for years.

- It was a relief for the patient to be unburdened with this.

- The result was that the patient would try to take the medication as prescribed by splitting the dose between two days returning after 3 months for follow up and change of treatment if necessary.
The Importance of Identifying Non-Compliance

- Why Should Non-Adherence be a problem?
- May not even be a problem if the patient can manage their disease and remain in remission
- Poor disease control which may lead to hospitalisation in some cases
- May lead to being prescribed biologics which has increased risk and cost
- Poor control of Side Effects
- Missing the chance to try something which may work better
- May not have an effective partnership for disease management with their Rheumatologist/Nurse
- Fundamentally better for us to have accurate information and we can learn from the patient experience
Adherence and patient education

- Nurses do a lot of the formal patient education

- The most universal and directly necessary education is around DMARD therapy

- The “consultation” involves the transfer of knowledge which is received in the context of the patient's experience and beliefs

- The aim is to improve patient concordance
National Survey

- identify the training that rheumatology nurses had received for educating patients about Methotrexate
- identify confidence in different aspects of this role
- evaluate knowledge around clinical situations relevant to Methotrexate use
- identify any need for additional training

## Training Method

<table>
<thead>
<tr>
<th>Main Training Method</th>
<th>Number of respondents (n= 73)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observing – other nurses and self directed</td>
<td>49  (67%)</td>
</tr>
<tr>
<td>Observing – Rheumatologists Clinics</td>
<td>8  (11%)</td>
</tr>
<tr>
<td>In-house chemotherapy course</td>
<td>7  (9.5%)</td>
</tr>
<tr>
<td>In-house competencies</td>
<td>4  (5.5%)</td>
</tr>
<tr>
<td>Rheumatology Course</td>
<td>4  (5.5%)</td>
</tr>
<tr>
<td>Prescribing Course</td>
<td>1  (1.4%)</td>
</tr>
</tbody>
</table>
## Confidence

<table>
<thead>
<tr>
<th>Confidence Level</th>
<th>Number of Respondents (n = 85)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very Confident</td>
<td>51 (60%)</td>
</tr>
<tr>
<td>Confident</td>
<td>20 (24%)</td>
</tr>
<tr>
<td>Somewhat Confident</td>
<td>10 (12%)</td>
</tr>
<tr>
<td>Not at all Confident</td>
<td>4 (5%)</td>
</tr>
</tbody>
</table>
Conclusions

- Nurses report confidence to educate patients about Methotrexate but it takes 3 – 12 months for most to achieve this.

- Nurses use a lot of prompts in the form of leaflets and checklists which may inhibit patients from asking questions.

- There is no “Gold Standard” training available, nurses have to be self motivated and resourceful in order to increase their education.

- Nurses are not taught consultation techniques which involves checking perceived knowledge at intervals.

An exploration of the experiences of rheumatology nurses counselling patients on methotrexate therapy
Sandra M. Robinson Sarah Ryan Nicola Adams Andrew Hassell David Walker
30 August 2018 Musculoskeletal Care https://doi.org/10.1002/msc.1361
BIOLOGICS

- Made by living cells
- More like a whisky than a chemical
- Large proteins (antibodies or receptors)
- Directed at components of the inflammatory cascade
- Expensive to make
- Difficult to copy (Bio-similars)
Anomalies:

- Some licenced for use only with Methotrexate
- Rituximab only after TNFi
- NICE can’t go against the licence
- Purchasers take a financial view
Co-morbidities

- If you don’t have anything that stops us treating you, then we have the tools to supress your arthritis.

- Infection risk is the biggest.
Co-Morbidities

- Interesting register data showing you are 5 x less likely to go into remission if your BMI is over 30!
- You are 2.5 x less likely to go into remission if you smoke!
- Swefot database
Conclusion

- Treatment of RA has improved beyond all recognition, both in strategy for use of conventional DMARDs and use of Biologics.
- Early Arthritis Clinics are here to stay.
- There are huge challenges keeping the patients on board.
- Patients who don’t need treatment tend to do very well on it!
Are we entering a Post Biologic Era?
Future therapeutic targets:

- IL-12/23
- IL-6
- IFNs
- IL-8
- TNF
- IL-1

Immune complexes

RA BEAM: Olumiant’s head-to-head trial vs adalimumab with background methotrexate (MTX)

In patients with moderate-to-severe RA who have had an inadequate response to MTX (MTX-IR)\(^1\)

RA-BEAM: Key inclusion and exclusion criteria

Key inclusion criteria

- Adult-onset RA, defined by ACR/EULAR 2010 criteria
- Inadequate response to MTX
- ≥ 3 erosions*
  * Patients with 1-2 erosions could enroll if rheumatoid factor or anti-citrullinated protein antibody was positive
- Stable background MTX
- ≥ 6/68 tender joints and ≥ 6/66 swollen joints
- hsCRP ≥ 6.0 mg/L

Key exclusion criteria

- Prior biologic DMARD use

RA-BEAM – ACR20 superiority over placebo

Olumiant achieved its primary endpoint - ACR20 superiority over placebo at Week 12
RA-BEAM – ACR20 superiority over placebo

Olumiant maintains superior efficacy vs placebo over 52 weeks.


RA-BEAM – ACR 20 superiority over Adalimumab at week 12

Olumiant + MTX demonstrated statistically significant improvements in efficacy vs Adalimumab + MTX at multiple time points over 52 weeks.


Rapid and sustained response – ACR50

Olumiant + MTX demonstrated statistically significant improvements in ACR50 compared with adalimumab + MTX at multiple time points from Week 8 to Week 52.


Rapid and sustained response – ACR20

Olumiant + MTX demonstrated statistically significant improvements in ACR20 compared with adalimumab + MTX at multiple time points from Week 12 to Week 52.


Rapid and sustained response – ACR70

Olumiant + MTX demonstrated statistically significant improvements in ACR70 compared with adalimumab + MTX at multiple time points from Week 8 to Week 40.


RA-BEAM – Patients achieving SDAI ≤11 or CDAI ≤10

Proportion of patients achieving SDAI ≤11 or CDAI ≤10 with Olumiant + MTX was superior to adalimumab + MTX at Week 12 and Week 52.

RA-BEAM: Safety
## Adverse event profile

Six placebo-controlled studies were integrated (997 patients on 4 mg Olumiant once daily and 1070 patients on placebo) to evaluate the safety of Olumiant in comparison to placebo for up to 16 weeks after treatment initiation.

<table>
<thead>
<tr>
<th>System organ class</th>
<th>Very common (≥1/10)</th>
<th>Common (≥1/100 to &lt;1/10)</th>
<th>Uncommon (≥1/1,000 to &lt;1/100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infections and infestations</td>
<td>Upper respiratory tract infections&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Herpes zoster</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Herpes simplex&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gastroenteritis</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Urinary tract infections</td>
<td></td>
</tr>
<tr>
<td>Blood and lymphatic system disorders</td>
<td></td>
<td>Thrombocytosis ≥600 x 10&lt;sup&gt;9&lt;/sup&gt; cells/L&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Neutropaenia &lt;1 x 10&lt;sup&gt;9&lt;/sup&gt; cells/L&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Metabolism and nutrition disorders</td>
<td>Hypercholesterolaemia&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td>Hypertriglyceridaemia&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>Nausea</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatobiliary disorders</td>
<td></td>
<td>ALT increased ≥3 x ULN&lt;sup&gt;c&lt;/sup&gt;</td>
<td>AST increased ≥3 x ULN&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td></td>
<td></td>
<td>Acne</td>
</tr>
<tr>
<td>Investigations</td>
<td></td>
<td></td>
<td>Weight increased</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Creatine phosphokinase increased ≥5 x ULN&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Please consult the summary of product characteristics for further details.

<sup>a</sup>Combined term (acute sinusitis, epiglottitis, laryngitis, nasopharyngitis, oropharyngeal pain, pharyngitis, pharyngotonsillitis, rhinitis, sinusitis, tonsillitis, tracheitis, upper respiratory tract infection)

<sup>b</sup>Combined term (eczema herpeticum, herpes simplex, ophthalmic herpes simplex, oral herpes)

<sup>c</sup>Includes changes detected during laboratory monitoring
## Adverse events overview: 0-24 Weeks

<table>
<thead>
<tr>
<th></th>
<th>RA-Beam¹ (MTX IR)</th>
<th>RA-Build² (cDMARD IR)</th>
<th>RA-Beacon³ (TNFi IR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of Patients</td>
<td>PBOᵃ N=488</td>
<td>ADAᵇ N=330</td>
<td>Bari 4 mgᵃ N=487</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Serious AEs (SAEs)ᵈ</td>
<td>5</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Serious infections</td>
<td>1 (&lt;1)</td>
<td>2 (&lt;1)</td>
<td>2</td>
</tr>
<tr>
<td>TEAEs</td>
<td>60</td>
<td>68</td>
<td>71</td>
</tr>
<tr>
<td>Discontinuation due to AE</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Infections</td>
<td>27</td>
<td>33</td>
<td>36</td>
</tr>
<tr>
<td>Herpes zoster</td>
<td>(&lt;1)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Malignancies, n (%)</td>
<td>3 (&lt;1)</td>
<td>0</td>
<td>2 (&lt;1)</td>
</tr>
<tr>
<td>NMSC, n (%)</td>
<td>1 (&lt;1)</td>
<td>0</td>
<td>2 (&lt;1)</td>
</tr>
<tr>
<td>MACE</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

ᵃParticipants taking background MTX therapy throughout the study.
ᵇBackground cDMARD required unless documented intolerance or contraindication
[cDMARD IR] [n=48 (7%)].
ᶜParticipants taking background cDMARD therapy throughout the study.
ᵈSAEs reported using conventional ICH definitions.

   doi:10.1136/annrheumdis-2016-210094
Olumiant showed no increased risk of malignancy (excluding NMSC) vs placebo or adalimumab + MTX at 24 weeks

Olumiant data presented in the above figure is combined data from Phase 2 and 3 placebo controlled studies in RA patients.

Olumiant data presented in above figures is combined data from Phase 1–3 studies in RA patients. Dose is an average of all exposures.

*Incidence rate was calculated as number of patients with event per 100 patient-years of observation time (including follow-up period) with observation time censored at the event start date CI=confidence interval; IR=incidence rate; PT YRS=patient-years.

Data on file: Olumiant safety information.
Olumiant showed no increased risk of serious infections vs placebo or adalimumab + MTX at 24 weeks\(^1\text{-}^3\)

**Serious infection by analysis set\(^1\text{-}^2\)**

**Incidence rate (95% CI) 100 patient-years**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Placebo</th>
<th>Olumiant 4 mg</th>
<th>Olumiant 2 mg</th>
<th>Olumiant 4 mg + MTX</th>
<th>Olumiant 4 mg + MTX</th>
<th>ADA + MTX</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALL PATIENTS</td>
<td>1070</td>
<td>997</td>
<td>479</td>
<td>479</td>
<td>488</td>
<td>487</td>
</tr>
<tr>
<td>WITH EVENTS</td>
<td>17</td>
<td>16</td>
<td>28</td>
<td>7</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>PATIENT-YEARS</td>
<td>403</td>
<td>417</td>
<td>480</td>
<td>551</td>
<td>201</td>
<td>217</td>
</tr>
</tbody>
</table>

**Serious infection incidence rates* and 95% CI by time periods – all patients treated with Olumiant in clinical trials\(^3\)**

**Incidence rate was calculated as number of patients with event per 100 patient-years of observation time (including follow-up period) with observation time censored at the event start date.**

CI = confidence interval; IR = incidence rate; PT YRS = patient-years.

Olumiant data presented in the above figure is combined data from Phase 2 and 3 placebo controlled studies in RA patients.

Olumiant data presented in above figures is combined data from Phase 1–3 studies in RA patients. Dose is an average of all exposures.

Data on file: Olumiant safety information.
The risk of herpes zoster was increased in patients treated with Olumiant vs placebo\textsuperscript{1–3}

Olumiant data presented in the above figure is combined data from Phase 2 and 3 placebo controlled studies in RA patients.

Olumiant data presented in above figures is combined data from Phase 1–3 studies in RA patients. Dose is an average of all exposures.

*Incidence rate was calculated as number of patients with event per 100 patient-years of observation time (including follow-up period) with observation time censored at the event start date.

CI=confidence interval; IR=incidence rate; PT YRS=patient-years.
Effect on Laboratory Values: 0-24 weeks

<table>
<thead>
<tr>
<th>CTCAE grade, n (%)</th>
<th>RA-BEAM&lt;sup&gt;1&lt;/sup&gt; (MTX IR)</th>
<th>RA-BUILD&lt;sup&gt;2&lt;/sup&gt; (cDMARD IR)</th>
<th>RA-BEACON&lt;sup&gt;3&lt;/sup&gt; (TNFi IR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low hemoglobin count</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 3: ≥6.5 to &lt;8.0 g/dL</td>
<td>1 (&lt;1)</td>
<td>0</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td>Low neutrophils count</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 3: &lt;1000 cells/mm&lt;sup&gt;3&lt;/sup&gt;</td>
<td>0</td>
<td>2 (&lt;1)</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td>Low lymphocytes count</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 3: ≥200 to &lt;500 cells/mm&lt;sup&gt;3&lt;/sup&gt;</td>
<td>9 (2)</td>
<td>4 (&lt;1)</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td>Elevated ALT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 3: &gt;5X ULN and ≤20X ULN</td>
<td>5 (1)</td>
<td>3 (&lt;1)</td>
<td>3 (&lt;1)</td>
</tr>
<tr>
<td>Elevated creatinine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 3: &gt;3X ULN and ≤6X ULN</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Data in table are n (%) patients, and indicate the worst common terminology criteria for adverse events grade in patients who experienced a treatment-emergent increase in grade at any time during the treatment period, up to the time of rescue. No patient discontinued study drug because of anemia. N = number of patients in the analysis.

Non-rescued PBO patients were switched to bari 4 mg QD at Week 24.

All patients on background MTX.


UKBAR00107 | June 2017 | © 2017 Eli Lilly and Company.
All rights reserved.
Taylor PC, et al. Oral Presentation American College of Rheumatology Annual Conference, 2015. Baricitinib Versus Placebo or Adalimumab in Patients with Active Rheumatoid Arthritis (RA) and an Inadequate Response to Background Methotrexate Therapy: Results of a Phase 3 Study.
## Laboratory Values

<table>
<thead>
<tr>
<th>Component</th>
<th>Description</th>
<th>Effects/Notes</th>
</tr>
</thead>
</table>
| **Lipids** | Increase across parameters; Plateau 12 weeks | - Increase responds to statin.  
- The effect of these elevations on the cardiovascular system has not been determined - no evident relation with MACE at the time of analysis. |
| **Liver** | ALT increase, with cDMARD background | - Most cases of hepatic transaminase elevations were asymptomatic and transient.  
- Increased similar to those seen with adalimumab.  
- Pattern and incidence of elevation in ALT/AST remained stable over time. |
| **CPK** | Dose-dependent increase | - Most cases were transient and did not require discontinuation.  
- No confirmed rhabdomyolysis  
- Elevations observed at 4 weeks and remained stable at higher value thereafter. |
| **Renal** | Very small creatinine increase | - Increase at 2 weeks, remained stable thereafter.  
- May be due to inhibition of creatinine secretion in renal tubules  
- Estimates of eGFR based on creatinine may be slightly reduced without actual loss of renal function of occurrence of adverse events. |

Hemoglobin < 8 g/dL was reported in less than 1% of patients in clinical trials.

Decreases similar to adalimumab.

No relationship with occurrence of serious infections.

Absolute Lymphocyte Count (ALC) < 0.5 x 10⁹ cells/L was reported in less than 1% of patients in clinical trials.

No association with AE of thrombotic nature.

Pattern and incidence remained stable at a higher value than baseline over time including in the long term extension study.

Practical use of Olumiant
65  Male, YOB 1948

Painter & Decorator, Hx L acromial neuralgia, presents with T & S MCPs & PIPs, EMS > 1hr, Rh F 217.

Clinical Trial BEGIN – Placebo/Baricitinib/MTX

Clinical Trial JADY – Open Label Baricitinib Mono Therapy
GP referral - ?RA, Pain & Swelling Hands, wrists, Shoulders, feet & Rt

MM Female, YOB 1942

- Sept 2006
  - RA, Pain & Swelling
  - Hands, wrists, Shoulders, feet & Rt

- Jan 2014
  - BEAM Clinical Trial – Baracitinib plus MTX

- Oct 2006
  - Cardera 2 – Anakinra/MTX
  - Declined

- March 2007
  - Kenalog 80mg

- Jan 2008
  - MTX 10mg

- Jul 2008
  - MTX 15mg
  - MTX 20mg

- Mar 2009
  - MTX 25mg

- Lost to follow up

- Jan 2014
- Sep 2015
- Jan 2017

- More active inflammation
  - TJC
  - SJC

- JADY Clinical Trial – Open Label Baracitinib plus MTX

- Methotrexate 25mg
JD 07/04/45 Civil Servant

SURGERY

- Left Knee SYNOVECTOMIES
- Right Knee SYNOVECTOMIES
- L TKR
- R TKR
- Wrist Replaced
- R Shoulder
- MCP L Shoulder
- Forefoot Arthroplasty
- R Elbow

STUDIES

- SIBSHIP Study
- MUR Study
- HUMIRA
- RITUXIMAB X 3

DAS SCORES

- Gold
- Penicillamine
- FROBEN AND COPROXAMOL
- MTX 10
- HUMIRA
- ETAN

Onset Seropositive RA
Symmetrical and Psoriasis

Rash
Psoriasis Worse
Improved sicca symptoms
Stopped Drops!

2012 2015 2018

Rash
Psoriasis Worse
Improved sicca symptoms
Stopped Drops!


< TRACE RA >