Psoriasis

Dr. Noemí Eirís Salvado
Complejo Asistencial Universitario de León
CARDIOVASCULAR DISEASE AND Ps
- Pianserico et al

MINOCA
(Myocardial infarction with non-obstructive coronary arteries)

ACUTE INVESTIGATION

- Coronary stenosis ≥50%
  - Treat as STEMI
- Urgent angiography
- No coronary stenosis ≥50% + Fulfilment universal AMI criteria

Acute LV wall motion assessment (angiogram / echo)

European Heart Journal (2018) 39, 119-17
Coronary Microvascular Dysfunction in Psoriasis
## Characteristics of Patients Before and After TNF-α Inhibitor Treatment

<table>
<thead>
<tr>
<th></th>
<th>Before TNF-α Inhibitor Treatment</th>
<th>After TNF-α Inhibitor Treatment</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PASI</td>
<td>17.5 ± 7.2</td>
<td>2.4 ± 3.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>hsCRP, mg/L</td>
<td>1.8 [0.3-3.3]</td>
<td>0.3 [0.12-2.6]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>IL-6, pg/ml</td>
<td>0 [0-1.5]</td>
<td>0 [0-0]</td>
<td>0.3</td>
</tr>
<tr>
<td>VEGF, pg/ml</td>
<td>313 [107-531]</td>
<td>126 [79-411]</td>
<td>0.6</td>
</tr>
<tr>
<td>TNF-α, pg/ml</td>
<td>9.9 [7.8-10.5]</td>
<td>4.4 [3-5]</td>
<td>0.001</td>
</tr>
<tr>
<td>CFR</td>
<td>2.2 ± 0.7</td>
<td>3.04 ± 0.8</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Mean ± SD or Median [range]

Pioserico S et al. Atherosclerosis 2016
CARDIOVASCULAR DISEASE AND Ps
- Mehta \textit{et al}
If the cardioprotective effects of the biological therapy occur without being reflected in a significant way in the most used inflammation markers ...... → At what level do they act?

VIP-E → Anti-TNF reduces systemic inflammation, neutral imaging effects

- Anti-TNF therapy had anti-inflammatory effects in the skin and blood of patients with psoriasis vs phototherapy

- Both anti-TNF therapy and phototherapy had neutral impact on VI as assessed by $^{18}$F-FDG PET/CT compared with placebo.

- Anti-TNF therapy had no impact on glucose metabolism with effects on reducing inflammatory biomarkers including GlycA, TNF-alpha and hs-CRP.

Mehta Lab NHLBI, Circulation CV Imaging, 2018.
Psoriasis → increased coronary plaque burden, which is *non-calcified*

<table>
<thead>
<tr>
<th>Coronary Plaque (mm²)</th>
<th>Psoriasis (n=105)</th>
<th>Healthy Volunteers (n=25)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Plaque Burden (X100)</td>
<td>1.22±0.31</td>
<td>1.04±0.22</td>
<td>0.001</td>
</tr>
<tr>
<td>Non-calcified Plaque Burden (X100)</td>
<td>1.18±0.32</td>
<td>1.03±0.21</td>
<td>0.004</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Unadjusted</th>
<th>Adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Burden</td>
<td>0.15 (&lt;0.001)</td>
<td>0.12 (0.01)</td>
</tr>
<tr>
<td>Non-calcified Burden</td>
<td>0.13 (0.003)</td>
<td>0.12 (0.01)</td>
</tr>
</tbody>
</table>

Adjusted for age, sex, SBP, LDL, HDL, Glucose, Current Smoking, Lipid Treatment

Garman et al., *Circulation*, 2017
High risk coronary plaque occurs over one decade earlier in psoriasis

<table>
<thead>
<tr>
<th>Coronary Plaque Type (mm²)</th>
<th>Psoriasis: age~46 (n=105)</th>
<th>Hyperlipidemia: age ~60 (n=100)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Plaque Burden (X100)</td>
<td>1.22±0.31</td>
<td>1.18±0.34</td>
<td>0.16</td>
</tr>
<tr>
<td>Non-calcified Plaque Burden (X100)</td>
<td>1.18±0.32</td>
<td>1.11±0.33</td>
<td>0.02</td>
</tr>
<tr>
<td>Presence of High-risk Plaque</td>
<td>36 (34%)</td>
<td>38 (38%)</td>
<td>0.58</td>
</tr>
</tbody>
</table>

Lerman et al., *Circulation*, 2017
If the cardioprotective effects of the biological therapy occur without being reflected in a significant way in the most used inflammation markers ...... → At what level do they act?
### Biologic Therapy (n=267 arteries)

<table>
<thead>
<tr>
<th>Coronary Plaque Type (mm²)</th>
<th>Baseline</th>
<th>One-Year</th>
<th>% change (P-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Plaque Burden (X100)</td>
<td>1.30±0.60</td>
<td>1.24±0.60</td>
<td>-5% (0.009)</td>
</tr>
<tr>
<td>Non-calcified Plaque Burden (X100)</td>
<td>1.22±0.60</td>
<td>1.15±0.59</td>
<td>-7% (0.005)</td>
</tr>
</tbody>
</table>

### Non-biologic Therapy (n=96 arteries)

<table>
<thead>
<tr>
<th>Coronary Plaque Type (mm²)</th>
<th>Baseline</th>
<th>One-Year</th>
<th>% change (P-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Plaque Burden (X100)</td>
<td>1.28±0.53</td>
<td>1.31±0.59</td>
<td>+2% (0.22)</td>
</tr>
<tr>
<td>Non-calcified Plaque Burden (X100)</td>
<td>1.19±0.41</td>
<td>1.25±0.41</td>
<td>+5% (0.17)</td>
</tr>
</tbody>
</table>

* Biologic therapy: anti-TNF, anti-IL12/23, anti-IL17

Elnabawi et al., CVR, 2019
High-risk plaque features decrease following biologic therapy

### Biologic Therapy (n=267 arteries)

<table>
<thead>
<tr>
<th>Coronary Plaque Type</th>
<th>Baseline</th>
<th>One-Year</th>
<th>% change (P-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibro-fatty Burden (mm²)</td>
<td>0.22±0.19</td>
<td>0.10±0.14</td>
<td>-55% (0.004)</td>
</tr>
<tr>
<td>Necrotic Core Burden (mm²)</td>
<td>0.07±0.19</td>
<td>0.03±0.19</td>
<td>-57% (0.03)</td>
</tr>
</tbody>
</table>

### Non-biologic Therapy (n=96 arteries)

<table>
<thead>
<tr>
<th>Coronary Plaque Type</th>
<th>Baseline</th>
<th>One-Year</th>
<th>% change (P-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibro-fatty Burden (mm²)</td>
<td>0.16±0.19</td>
<td>0.22±0.14</td>
<td>+38% (0.004)</td>
</tr>
<tr>
<td>Necrotic Core Burden (mm²)</td>
<td>0.06±0.19</td>
<td>0.08±0.19</td>
<td>+33% (0.27)</td>
</tr>
</tbody>
</table>

* Biologic therapy: anti-TNF, anti-IL12/23, anti-IL17

Elnabawi et al., CVR, 2019
Subgroup analysis by biologic therapy

**Anti-TNF Therapy (n=48)**

<table>
<thead>
<tr>
<th>Coronary Plaque Type (mm²)</th>
<th>Baseline</th>
<th>One-Year</th>
<th>% change (P-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Plaque Burden (X100)</td>
<td>1.37±0.60</td>
<td>1.31±0.59</td>
<td>-4% (0.09)</td>
</tr>
<tr>
<td>Non-calcified Plaque Burden (X100)</td>
<td>1.28±0.60</td>
<td>1.22±0.59</td>
<td>-5% (0.06)</td>
</tr>
</tbody>
</table>

**Anti-IL17 Therapy (n=22)**

<table>
<thead>
<tr>
<th>Coronary Plaque Type (mm²)</th>
<th>Baseline</th>
<th>One-Year</th>
<th>% change (P-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Plaque Burden (X100)</td>
<td>1.31±0.60</td>
<td>1.15±0.59</td>
<td>-16% (0.0001)</td>
</tr>
<tr>
<td>Non-calcified Plaque Burden (X100)</td>
<td>1.23±0.58</td>
<td>1.08±0.57</td>
<td>-12% (0.001)</td>
</tr>
</tbody>
</table>

Elnabawi et al., CVR, 2019
New Combinations in psoriasis: halobetasol and tazarotene

- Two multicenter, randomized, double-blind, vehicle-controlled phase 3 studies (N = 418)
- At least a 2-grade improvement from baseline in Investigator’s Global Assessment score and a score of clear or almost clear).
- 35.8% (study 1) and 45.3% (study 2) of subjects were treatment successes compared with 7.0% and 12.5% of those treated with vehicle (P<.001).

Slides provided by Dr. JM Carrascosa
TAPINAROF (GSK2894512 CREAM) FOR THE TREATMENT OF PLAQUE PSORIASIS

- Nonsteroidal topical agent known as therapeutic aryl hydrocarbon receptor (AhR) modulating agents.
- Binding the AhR and activating the AhR pathway in multiple cells and tissue-based systems
- Controls the expression of IL-21 and IL-22 and plays an important role in the differentiation of T-helper 17 cells in vivo and in vitro
- Antioxidant by inhibiting reactive oxygen species

Slides provided by Dr. JM Carrascosa
PGA 0 or 1 and a 2-grade improvement at week 12 was statistically significantly higher (at a .05 significance level) in the tapinarof groups (65% [1% twice daily], 56% [1% once daily], 46% [0.5% twice daily], and 36% [0.5% once daily]) than in the vehicle groups (11% [twice daily] and 5% [once daily])

Slides provided by Dr. JM Carrascosa
Adalimumab/Certolizumab – new data

• pregnancy
• Analysis of about **2100 prospectively documented pregnancies** exposed to adalimumab and with live births with known outcome showed no evidence for an increased rate of malformations in newborns. (1500/1.trimester)

• Data from > **500 prospectively collected pregnancies** (400/1.trimester), give evidence, that Certolizumab has no harmful effect on malformations

• lactation
• Data from literature show that adalimumab can be excreted into breast milk resulting in low concentrations (0,1 – 1 % of maternal serum level). After oral ingestion follows intestinal proteolysis → low bioavailability → no negative effect on breast-fed infant expected

• Certolizumab can be used during lactation

https://www.gelbe-liste.de/produkte/Cimzia-200-mg-Injektionsloesung-In-einem-Fertigpen_972925/fachinformation
https://www.gelbe-liste.de/produkte/Humira-40-mg-0-4-ml-Injektionsloesung-im-Fertigpen_952401/fachinformation
Anti-TNF in elderly patients?

- n=145, ≥65 years, biologic naive, PsA
- ETA n=68, ADA n=60, Go n=11, IFX n=6
- MDA T6 22.6%, T12 51.8%
- Drug discontinuation rate 5.5%, mean 6.8 months due to lack of efficacy, AE or lost to FU
- N=9 (6.2%) mild infections treated with antimicrobials without therapy interruption
- ↓ age should not be considered a limitation to their use

MDA = minimal disease activity

Biologics (anti-TNF) and elderly patients

- IMIDs - inflammatory bowel disease, rheumatoid arthritis, psoriasis; > 60 years
- meta-analysis 14 studies with n = 4719 older users of biologics, n=13,305 young users of biologics, and n= 3961 older patients who did not use biologics.
- pooled prevalence of infections: 13% in older and 6% in younger users of biologics → OR 2.28 (95% CI, 1.57-3.31)
- Older users of biologics had a 3-fold increase in risk of infection compared to patients who did not use biologics (OR, 3.60; 95% CI, 1.62-8.01)
- older age: significant increase in risk of malignancy (OR, 3.07; 95% CI, 1.98-4.62) compared to younger age
- no significant differences in odds of malignancy (0.54, 95% CI, 0.28-1.05) or death (OR, 1.52; 95% CI, 0.44-5.28) compared to older patients who did not use biologics.
DRUGS - ANTI TNF AND SMALL MOLECULES

• Small molecules →
  • Tofacitinib →

Tofacitinib – efficacy and safety

Safety:
- Diarrhea, headache, dyslipidemia, elevated liver enzymes
- Bacterial Infections, urogenital; Herpes zoster
- Anemia… Increase of CK, Hypertension
DRUGS - ANTI TNF AND SMALL MOLECULES

- Small molecules →
  - Baricitinib →


Safety
Infections 26.5 (Plc) vs 21.1% (baricitinib)
Most frequent nasopharyngitis
No opportunistic infections
More laboratory AEs (9.3% vs 0%):
  Most frequent: increased CK
Higher rate of AEs in 8- and 10-mg-groups
DRUGS - ANTI TNF AND SMALL MOLECULES

• Small molecules →
  • TYK2-Inhibitors →
DRUGS - ANTI TNF AND SMALL MOLECULES

- Small molecules
  - TYK2-Inhibitors

New therapy with TYK2-Inhibitors?

- Preliminary but reassuring safety data suggest that TYK2 inhibition with BMS-986165 is selective and well tolerated.
- Presence of acne is of note, and has been seen with other agents that block this pathway.
DRUGS - ANTI TNF AND SMALL MOLECULES

• Small molecules ➔
  • Apremilast ➔

Poster 9879 – Apremilast – pediatric psoriasis

- n=42
- PASI score, mean (SD) 18.8 (11.7) 15.7 (3.4) 18.1 (6.1)
- group 1 (12-17y), BW ≥35 to <70 kg received APR20;
- group 2 (6-11y), BW ≥15 kg received APR20.

Inclusion criteria
Pediatric patients from 6 to 17 years
moderate to severe plaque psoriasis: PASI score ≥12, BSA ≥10%, sPGA ≥3, for ≥6 months
No sufficient control by topical therapy, candidate for systemic therapy/phototherapy
Previous therapy: ≤1 systemic therapy for psoriasis
(NO titration of dosage!)

Paller A et al. Poster 9879 AAD 2019
GRACIAS