

Clinical Data TDM CERTOLIZUMAB

Bensoussan Julien

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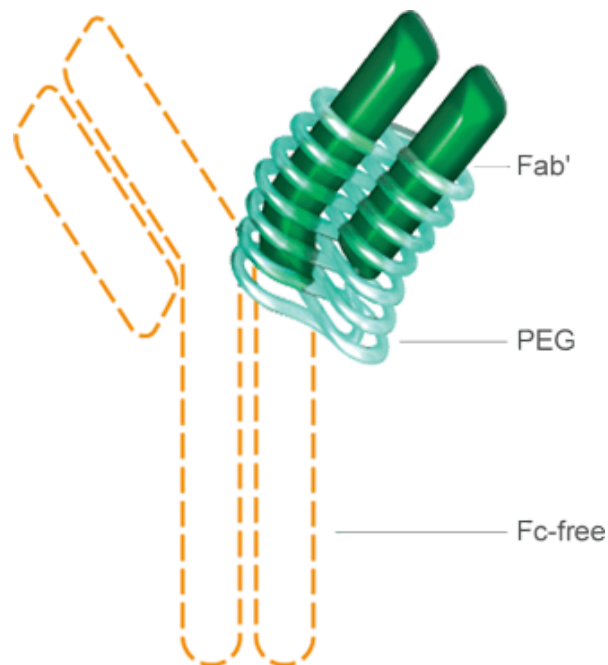
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Introduction





CIMZIA—PEGylated Fab' (TNF) inhibitor

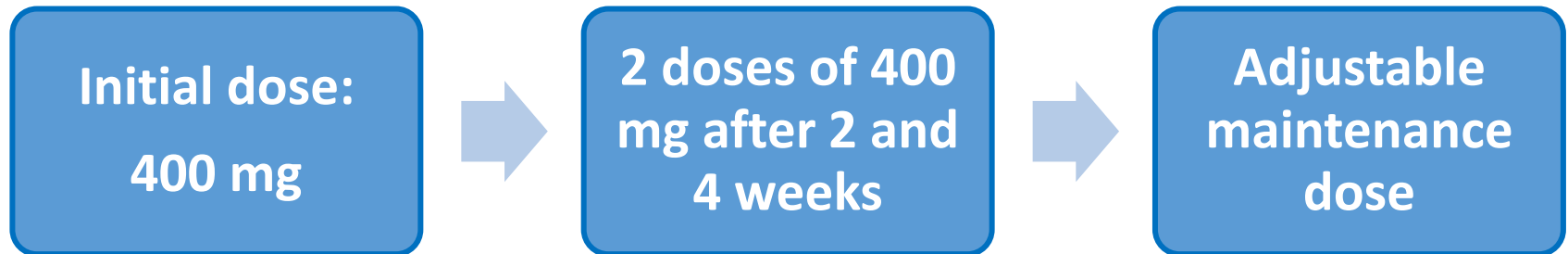
CERTOLIZUMAB PEGOL :

- Fab' fragment of a humanized antibody coupled to polyethylene glycol (PEG)
- **Target:** TNF α
- **Brand name:** Cimzia[®]
- **Marketed by** 
- FDA 2008 / EMA 2009
- About 15,000 patients treated (*data monitor 2018*)
- End of the patent: 2022 US / 2021 EU

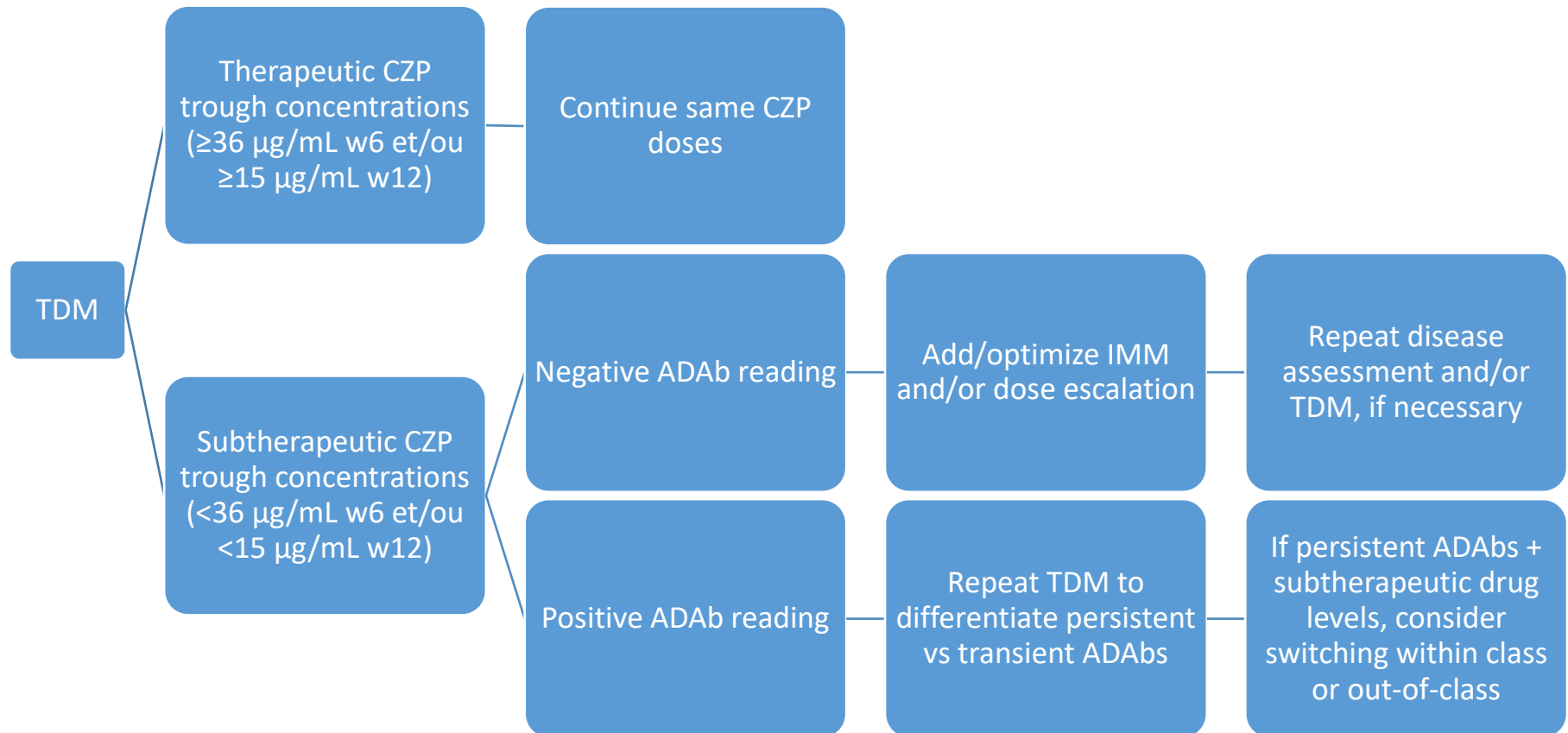
- Rheumatoid arthritis
- Psoriatic arthritis
- Axial Spondylitis
- Plaque psoriasis

- **US, Canada, Switzerland** → Indication for adult Crohn's disease
- **France** → prescription outside the marketing authorization under conditions:
 - ✓ Reserved for patients with relapsing Crohn's disease despite the use of all available treatments: corticosteroids, immunosuppressants, infliximab and adalimumab as well as vedolizumab and ustekinumab
 - ✓ The patient must be informed that this drug is prescribed outside the marketing authorization
 - ✓ The bibliography of Certolizumab in Crohn's disease must be documented in the medical record

Certolizumab Pegol : CIMZIA[®] - GETAID
CIMZIA - VIDAL



In the treatment of rheumatoid arthritis and psoriatic arthritis, this drug is sometimes combined with methotrexate.



Van de Castele et al.
[izaa265.pdf \(nih.gov\)](#)



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Clinical studies



Therapeutic Drug Monitoring of Tumor Necrosis Factor Antagonists in Crohn Disease: A Theoretical Construct to Apply Pharmacokinetics and Guidelines to Clinical Practice

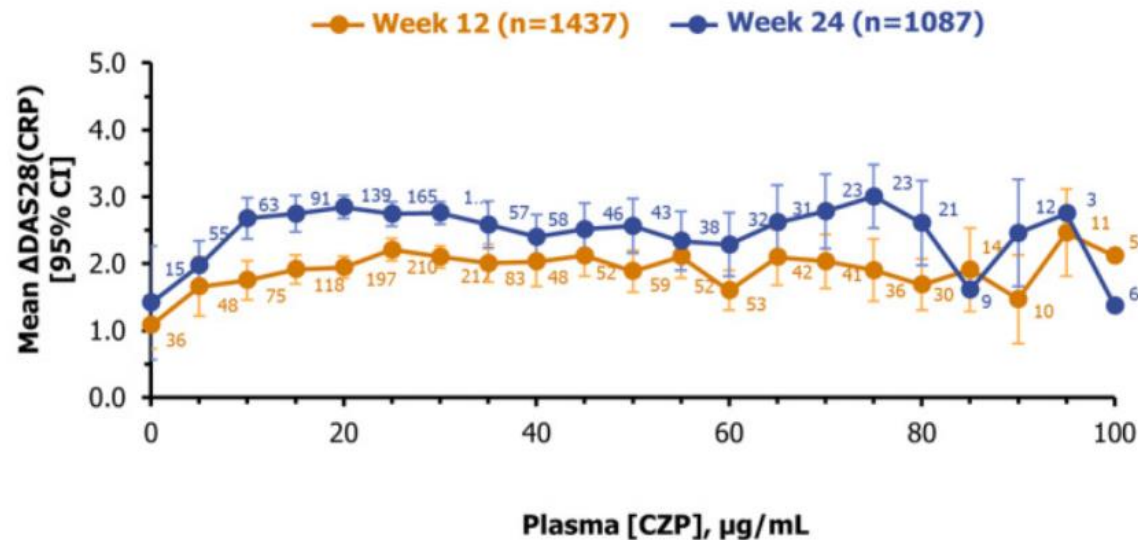
- **Aims:** To provide an overview of assays and guidelines on TDM and of clinical studies investigating TDM of TNF antagonists, in particular infliximab, adalimumab, and **certolizumab pegol**, for the treatment of **CD**, and to provide practical advice for clinicians on the use of both **reactive and proactive TDM**.
- **Results:**
 - ✓ **CZP concentrations and CZP ADABs correlate with clinical outcomes** in patients with CD
 - ✓ **Higher CZP serum concentrations (week 8) were associated with endoscopic response and clinical remission (week 10)** in patients with CD. At week 54, the rates of endoscopic remission correlated with CZP plasma concentrations
 - ✓ CZP trough concentrations **>27.5 µg/mL** were associated with radiological healing, radiological response, and symptomatic response
 - ✓ Lower trough concentrations (**<27.5 µg/mL**) were significantly associated with changes in clinical management

CZP concentrations of 36 µg/mL at week 6 and 15 µg/mL at week 12 were associated with attainment of a robust combined efficacy outcome at week 26

Van de Castele et al - 2021 - Inflamm Bowel Dis

Exposure-Response Relationship of Certolizumab Pegol and Achievement of Low Disease Activity and Remission in Patients With Rheumatoid Arthritis

- **Aims:** To identify minimum plasma concentrations of the anti-TNF certolizumab pegol (CZP) associated with improvement of disease activity in patients with RA during treatment with approved doses of CZP.
- **Results:** Plasma CZP concentrations < 10 µg/mL were generally associated with smaller improvements from baseline in DAS28(CRP) compared with patients with higher CZP concentrations.



- An association between CZP plasma concentration and clinical outcomes of low disease activity (LDA) and remission was observed.
- CZP concentration cutoffs of 28.0 µg/ml at week 12 and 17.6 µg/ml at week 24 were associated with a greater likelihood of achieving LDA and remission.

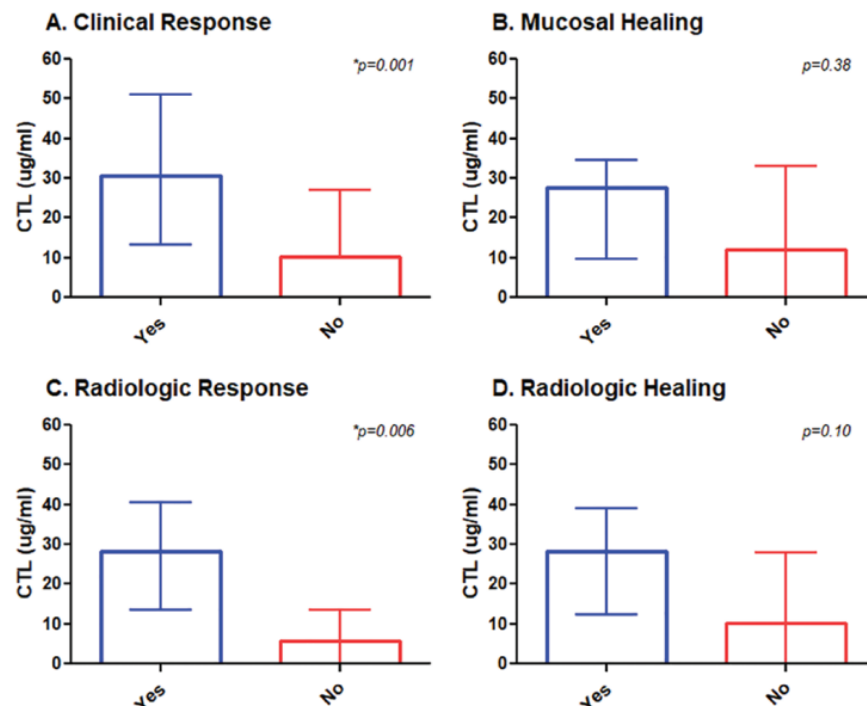
Paul et al - 2020 - Clin Transl Sci

Certolizumab Trough Levels and Antibodies in Crohn Disease: A Single-Center Experience

- **Aims:** To correlate CZP trough levels (CTLs) with Crohn Disease outcomes and to determine frequency of CZP antibodies.

- **Results:**

Median CTL was 18.9 µg/mL. Median CTL levels were higher in patients with vs without CR (30.4 vs 10.3 µg/mL) and RR (29.6 vs 5.8 µg/mL). CZP dosing at least every 2 weeks was associated with higher odds of achieving MH. CTL resulted in change in clinical management in 62.7% of cases. Receiver operating characteristic curve and quartile analysis suggested that CTL >19 µg/mL is associated with increased rates of CR and RR.

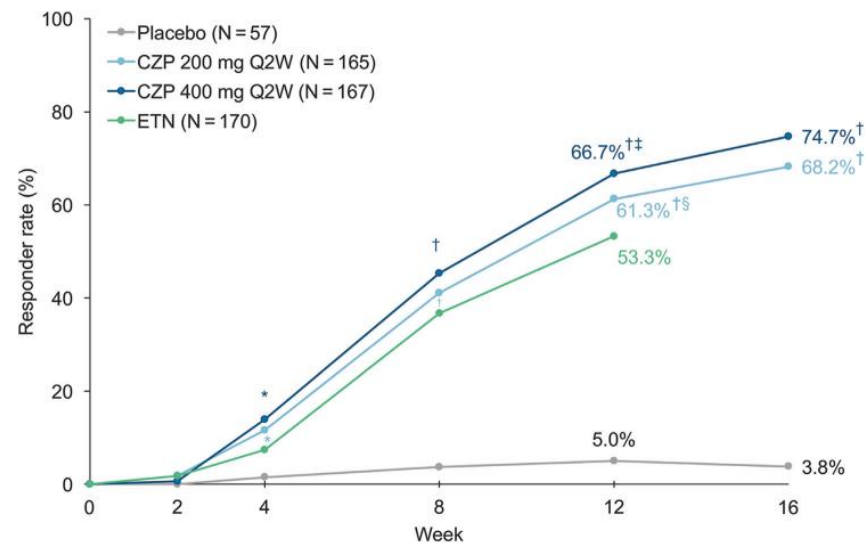


Higher CTL was significantly associated with CR and RR. The rate of CZP antibodies was 27.3%. Our data suggest maintenance CTL of ≥ 19 µg/mL should be achieved in order to optimize outcomes in clinical practice

Ramos et al - 2021 - Crohn's & Colitis 360

Certolizumab pegol for the treatment of chronic plaque psoriasis: Results through 48 weeks of a phase 3, multicenter, randomized, double-blind, etanercept- and placebo-controlled study (CIMPACT)

- **Aims:** Assess safety and efficacy of certolizumab in adults with moderate-to-severe chronic plaque psoriasis.
- **Results:** All endpoints were significantly greater for CZP versus placebo with the greatest response seen with 400 mg. CZP 400 mg was superior to and 200 mg was noninferior to etanercept. Adverse events were consistent with the antitumor necrosis factor class of drugs.

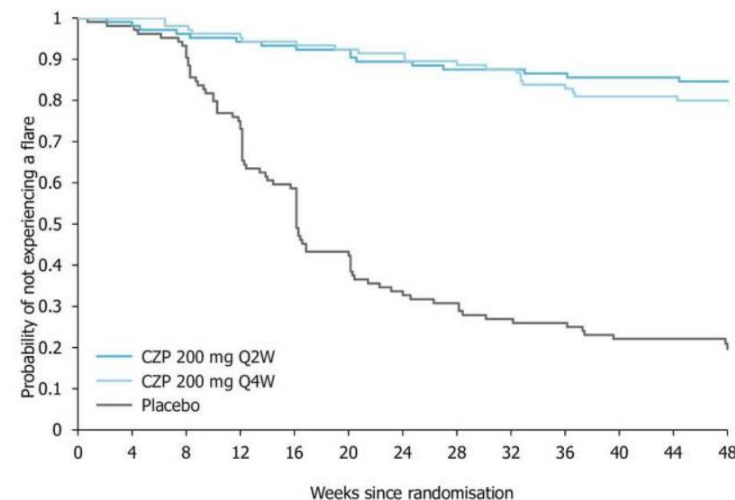
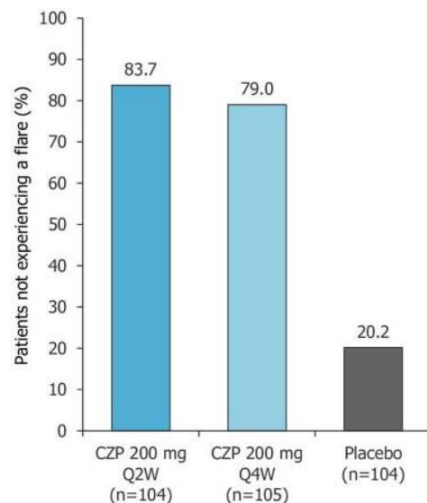


Both certolizumab regimens improved psoriasis symptoms, with a greater response seen with the higher dose.

Lebwohl et al - J Am Acad Dermatol - 2018

Maintenance of clinical remission in early axial spondyloarthritis following certolizumab pegol dose reduction

- **Aims:** C-OPTIMISE compared dose continuation, reduction and withdrawal of the tumour necrosis factor inhibitor certolizumab pegol (CZP) following achievement of sustained remission in patients with early axSpA.
- **Results:** At Week 48, 43.9% patients achieved sustained remission, of whom 313 were randomized to CZP full maintenance dose, CZP reduced maintenance dose or placebo. During Weeks 48 to 96, 83.7%, 79.0% and 20.2% of patients receiving the full maintenance dose, reduced maintenance dose or placebo, respectively, were flare-free.



Patients with early axSpA who achieve sustained remission at 48 weeks can reduce their CZP maintenance dose; however, treatment should not be completely discontinued due to the high risk of flare following CZP withdrawal.

Landewé et al - Ann Rheum Dis - 2020



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Take home messages



- ✓ **Certolizumab Pegol or Cimzia®** → Fab' fragment of a humanized antibody coupled to polyethylene glycol (PEG)
- ✓ **Indications** → Rheumatoid arthritis, Psoriatic arthritis, Axial Spondylitis, Plaque psoriasis
- ✓ **Posology**

Initial dose		Maintenance dose
400 mg	2 doses of 400 mg after 2 and 4 weeks	Adjustable

- ✓ **Cut-off** → **36 µg/mL** at week 6 and **15 µg/mL** at week 12 (Van de Casteele et al - 2021)
→ **28.0 µg/mL** at week 12 and **17.6 µg/mL** at week 24 (Paul et al - 2020)