

What's new in vasculitis
research?...*future treatments*

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Overview: ANCA-associated vasculitis

- What are the challenges?
 - Non-toxic, effective treatments
 - Earlier diagnosis at 1st presentation and relapse
 - Animal models
- A move towards designer biologic therapies
 - Targeting B cells
 - Targeting T cells

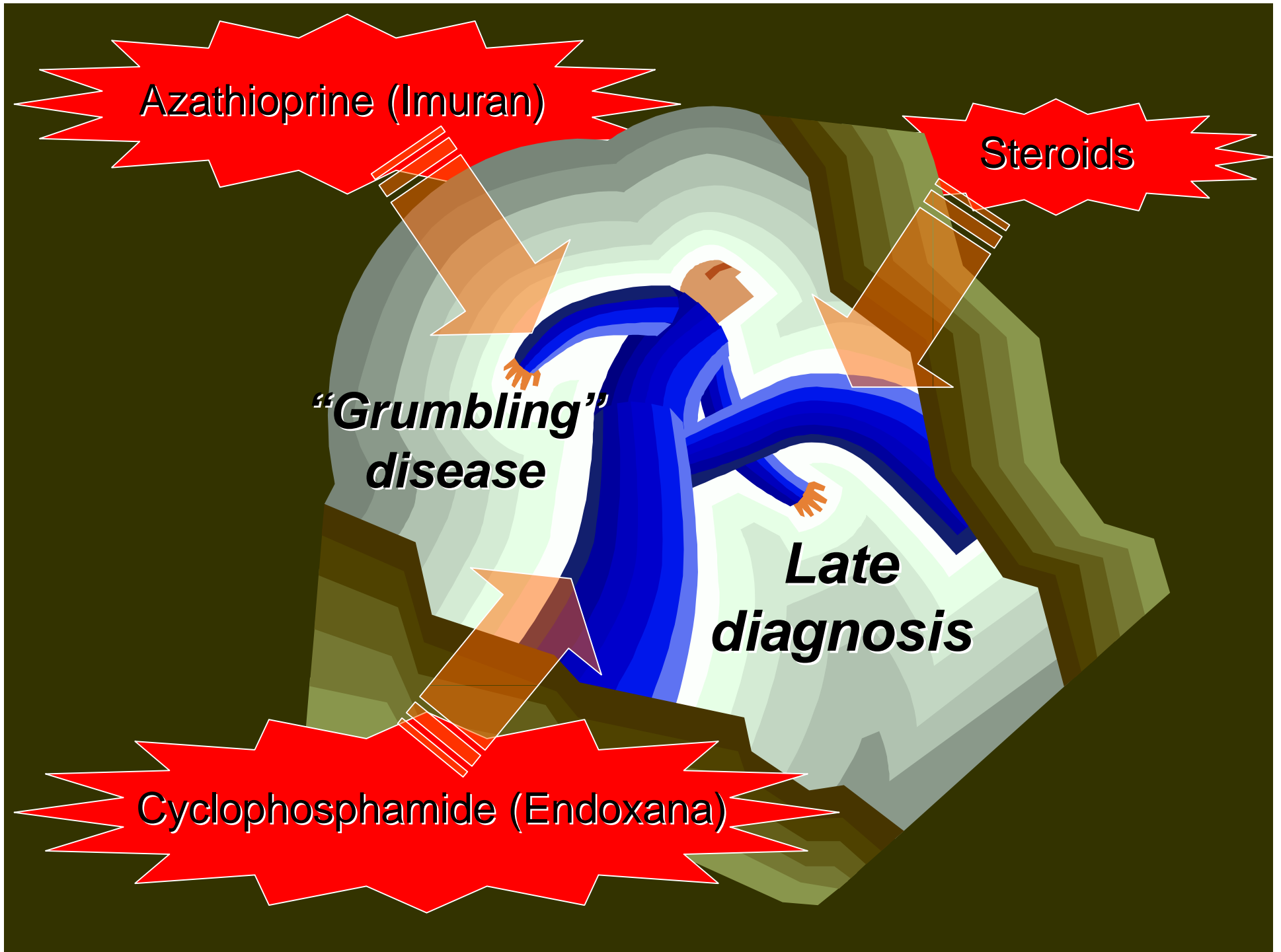
Azathioprine (Imuran)

Steroids

***“Grumbling”
disease***

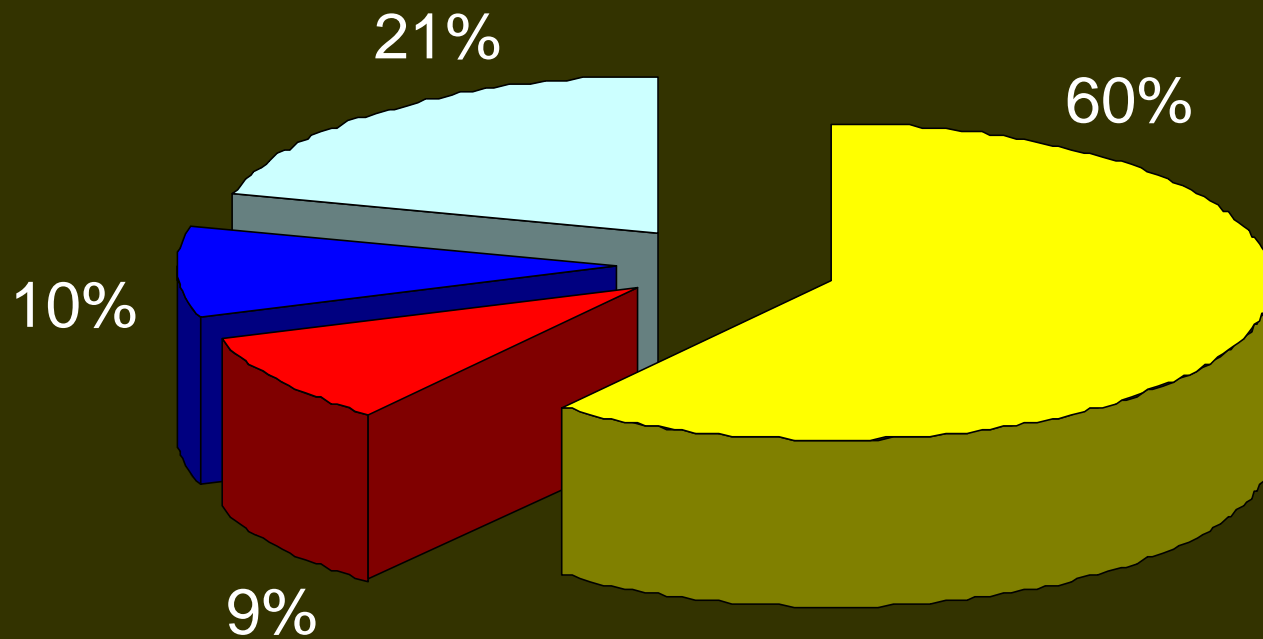
***Late
diagnosis***

Cyclophosphamide (Endoxana)



Cause of death in 43 of 368 patients enrolled in the EUVAS trials

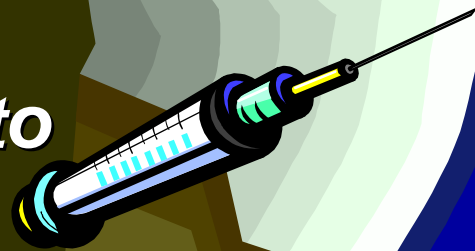
- Active vasculitis
- Heart disease
- Other
- Infection



Diagnostic techniques that allow treatment
before **tissue destruction** occurs



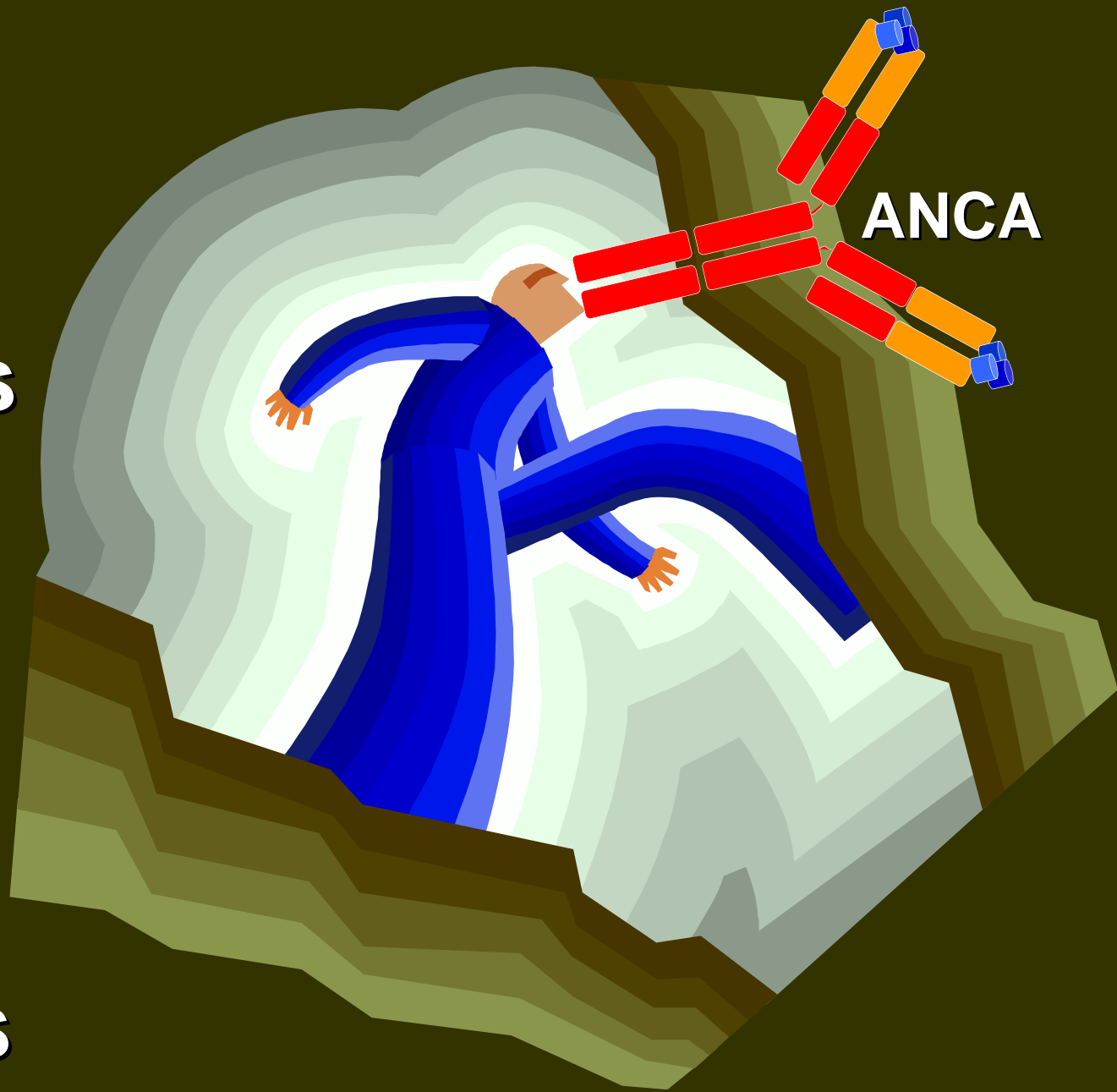
Specific
therapy
designed to
target the
underlying
defect in
vasculitis



B-cells

T-cells

ANCA



Part mouse, Part human



Rituximab
(Rituxan
Mabthera)

Knocks out
B cells



Originally used
for lymph
cancers and
rheumatoid
arthritis



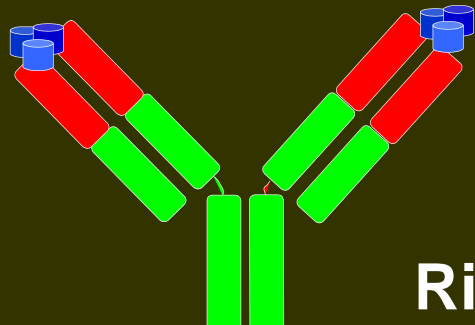
Usually given as 2 injections, 2
weeks apart



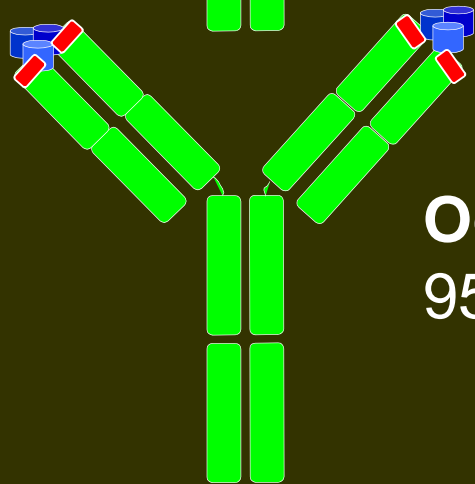
1 million
patients treated



Rituximab: taking out the mouse



Rituximab: 65% human (Chimeric)

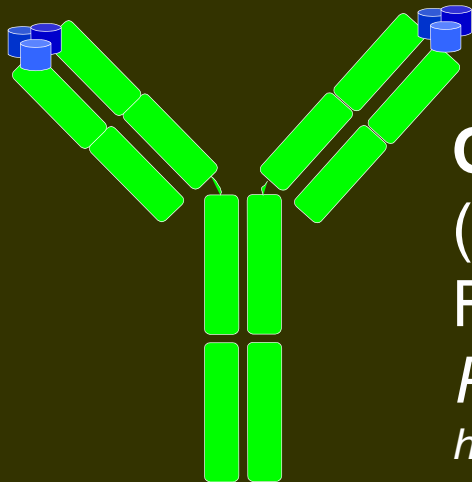


Ocrelizumab (Genentech / Roche):
95% human

*Being tested in 1000 patients with
Rheumatoid arthritis (Phase III)*

<http://clinicaltrials.gov/show/NCT00406419>

Rituximab: taking out the mouse



Ofatumumab *oh-FAT-oo-moo-mab*

(HuMax CD20, GSK / Genmab):

Fully human

Phase II trials

<http://www.genmab.com/ScienceAndResearch/ProductsinDevelopment/HuMax-CD20>



Tru-015 (Trubion / Wyeth)

Phase II trials

http://www.biospace.com/news_story.aspx?NewsEntityId=69298

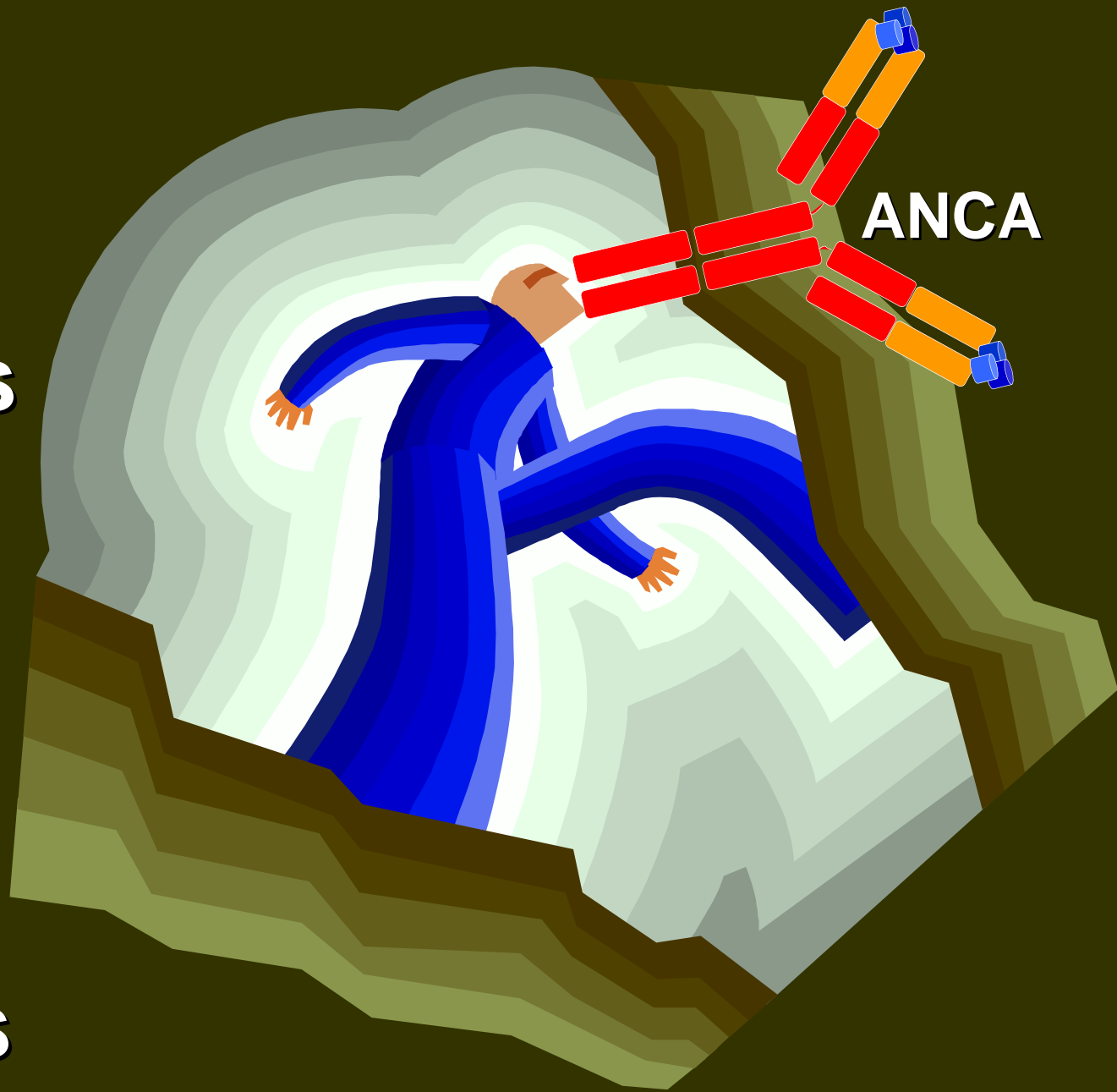
Blocking BLyS

- **Belimumab** (Lymphostat-B):
 - Human Genome Sciences / GSK
 - <http://www.hgsi.com/products/LSB.html>
 - In Phase III clinical trials in SLE
- **Atacicept**: TACI blocker:
 - Zymogenetics and Serono/Merck (Phase II)
 - <http://www.zymogenetics.com/products/taci-ig.html>
- **BR3-Fc**: BAFF blocker: Biogen / Genentech

B-cells

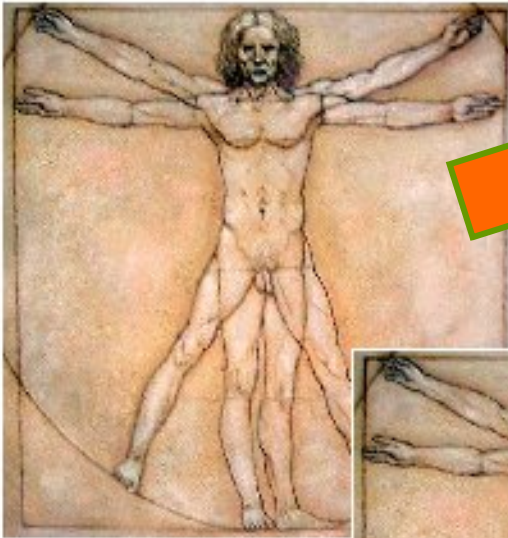
T-cells

ANCA



Abatacept (Orencia)

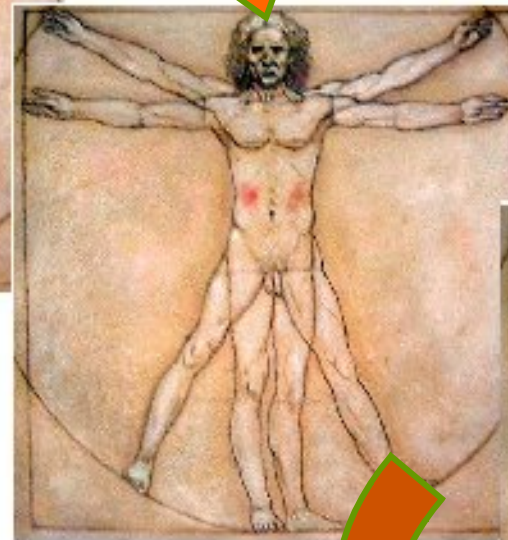
- Only targets T-cells that are activated to cause damage and makes them “anergic”
- Potential to be a highly selective therapy
- Currently undergoing Phase III study
 - ABAVAS, *Bristol Myers Squibb*
<http://clinicaltrials.gov/ct/gui/show/NCT00482066;jsessionid=53D839FB9C1A11598084022EA6A8092B?order=14>



Late diagnosis



Grumbling disease



Unrecognised relapse

“Biomarkers”

