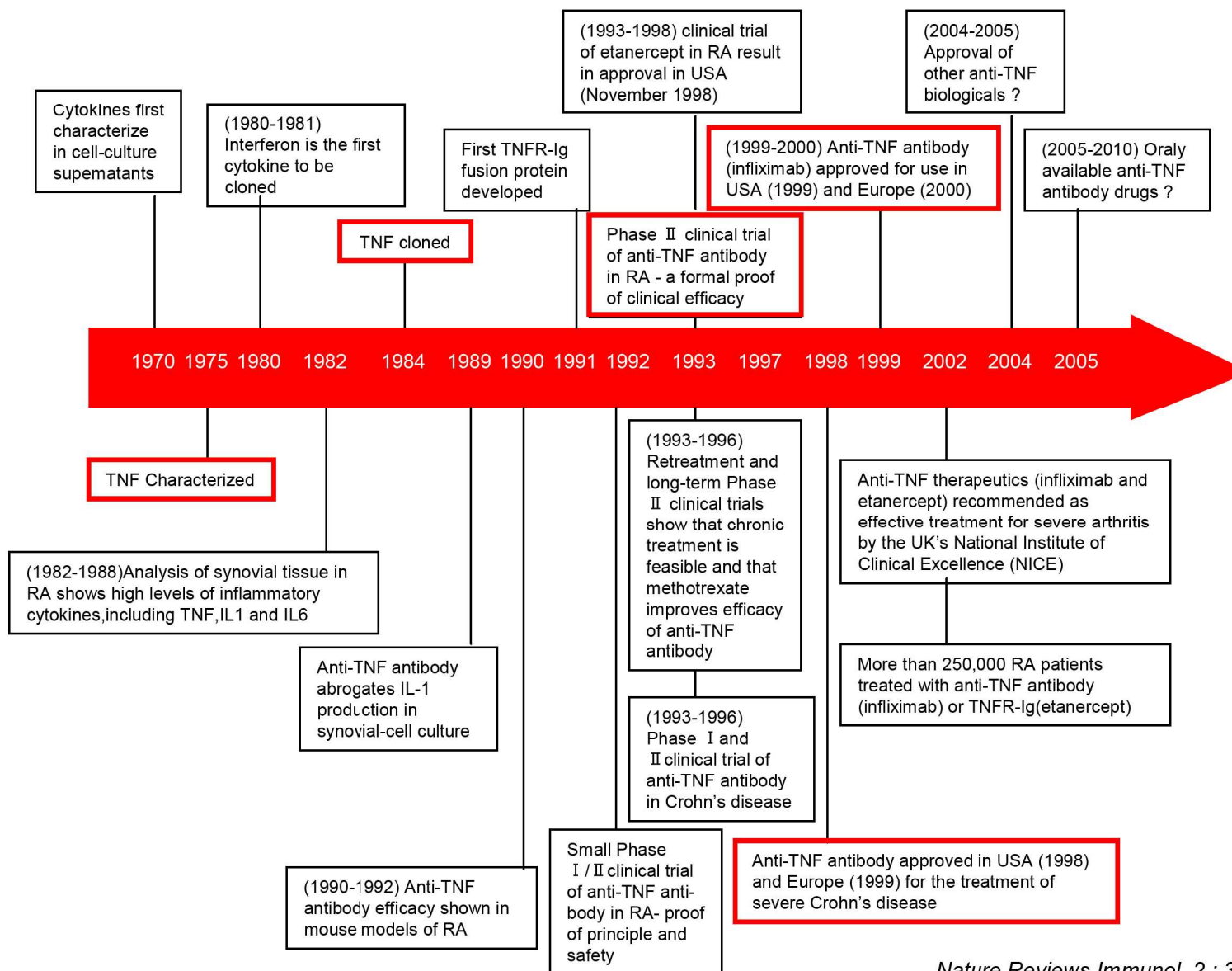


Development of anti-TNF therapy for chronic inflammatory disease



REVIEWS IN BASIC AND CLINICAL GASTROENTEROLOGY

John P. Lynch and David C. Metz, Section Editors

Biological Therapies for Inflammatory Bowel Diseases

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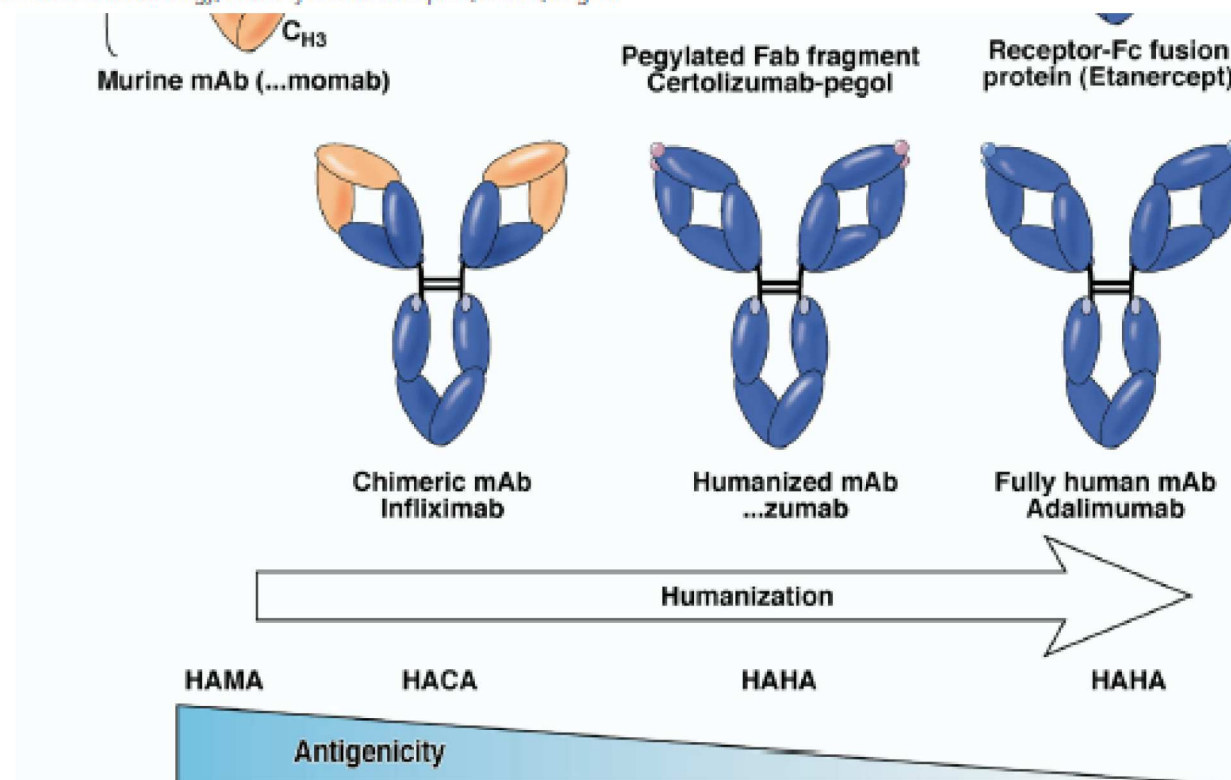


Figure 1. Humanization of therapeutic antibodies illustrated with the anti-TNF agents used in clinical practice. Original mouse IgG1 monoclonal antibodies (mAbs) contain mouse sequences only in every part of the variable (V) and constant (C) regions of both light (L) and heavy (H) chains. The 2 heavy chains are connected by the glycosylated hinge region, which separates the antibody binding Fab region from the effector, or complement

Hepatosplenic T cell lymphoma in inflammatory bowel disease

Matthew Shale,¹ Ed Kanfer,² Remo Panaccione,³ Subrata Ghosh¹

Table 1 Cases of hepatosplenic T cell lymphoma (HSTCL) reported in patients treated with anti-TNF drugs

| Case | Diagnosis | Anti-TNF | Concomitant therapy | Age | Sex | Outcome | Notes |
|------|-----------|-----------|---------------------|-----|-----|---------|---|
| 1* | CD | IFX | 6-MP, steroids | 31 | M | Death | Treated with chemotherapy and SCT |
| 2* | CD | IFX | AZA, steroids | 15 | M | Death | Treated with chemotherapy |
| 3* | CD | IFX | AZA | 12 | M | Death | Treated with chemotherapy |
| 4* | CD | IFX | 6-MP, steroids | 17 | F | Death | Treated with chemotherapy |
| 5* | CD | IFX | AZA, 6-MP, steroids | 19 | M | Death | Treated with chemotherapy and SCT |
| 6* | CD | IFX | AZA, 6-MP, steroids | 18 | M | Death | Treated with chemotherapy |
| 7* | CD | IFX | AZA | 19 | M | Death | Treated with chemotherapy and SCT |
| 8* | UC | IFX | AZA, steroids | 22 | M | Death | Treated with chemotherapy and BMT |
| 9 | RA | ADA | Steroids | 61 | F | Death | First HSTCL with anti-TNF not in IBD patient Patient not reported to be receiving thiopurine therapy |
| 10 | UC | IFX + ADA | 6-MP | 21 | M | Death | – |
| 11 | CD | IFX + ADA | AZA | 29 | M | Unknown | Treated with chemotherapy and BMT |
| 12 | CD | IFX | 6-MP, steroids | 22 | M | Death | Treated with chemotherapy |
| 13 | CD | IFX | 6-MP, steroids | 31 | M | Death | Treated with chemotherapy |
| 14 | CD | IFX | 6-MP, AZA, steroids | 31 | M | Death | Treated with chemotherapy |
| 15 | CD | IFX | AZA, steroids | 40 | M | Death | Treated with chemotherapy and BMT |
| 16 | CD | IFX | 6-MP | 19 | M | Death | – |
| 17 | UC | IFX | AZA | 58 | M | Unknown | Oldest reported HSTCL in IBD patient |

*Cases 1–8 were previously reported by Mackey *et al.*²⁴ Data derived from Mackey *et al.*,¹⁴ US Food and Drug Administration²⁵ and personal communication with Schering-Plough, Welwyn Garden City, UK. Some observations are missing from reports. ADA, adalimumab; AZA, azathioprine; BMT, bone marrow transplant; CD, Crohn's disease; F, female; IBD, inflammatory bowel disease; IFX, infliximab; M, male; 6-MP, 6-mercaptopurine; RA, rheumatoid arthritis; SCT, stem cell transplant; TNF, tumour necrosis virus; UC, ulcerative colitis.

ORIGINAL ARTICLE

Infliximab, Azathioprine, or Combination Therapy for Crohn's Disease

Jean Frédéric Colombel, M.D., William J. Sandborn, M.D., Walter Reinisch, M.D., Gerassimos J. Mantzaris, M.D., Ph.D., Asher Kornbluth, M.D., Daniel Rachmilewitz, M.D., Simon Lichtiger, M.D., Geert D'Haens, M.D., Ph.D., Robert H. Diamond, M.D., Delma L. Broussard, M.D., Kezhen L. Tang, Ph.D., C. Janneke van der Woude, M.D., Ph.D., and Paul Rutgeerts, M.D., Ph.D., for the SONIC Study Group*

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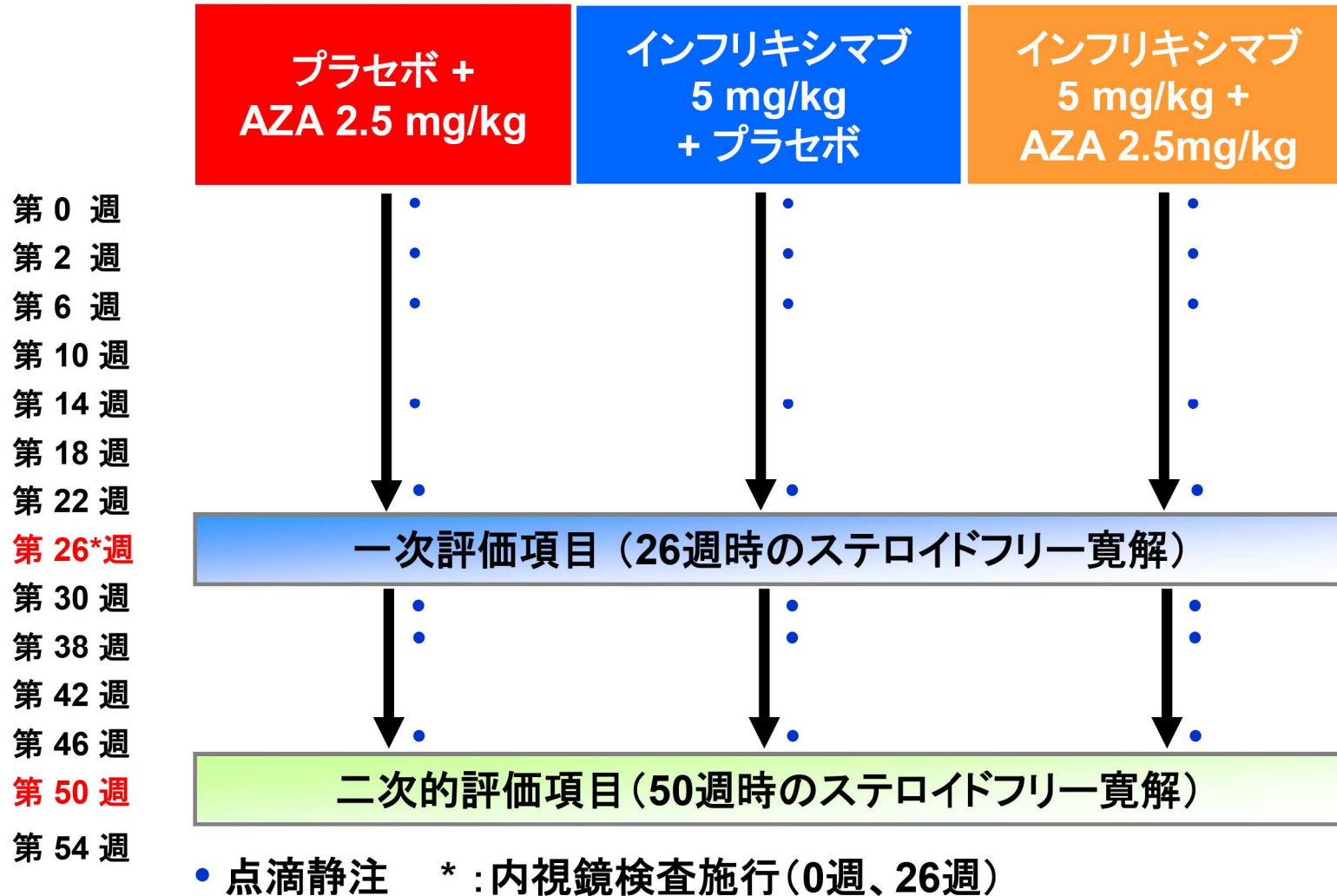
The **S**udy **o**f Biologic and Immunomodulator **N**aive Patients **i**n **C**rohn's Disease

- ・ 免疫調節剤および生物学的製剤未使用のクローン病患者に対するAZA単独、IFX単独、またはIFX+AZA併用療法による無作為二重盲検比較試験

登録患者

- 21歳以上の患者
- 中等度から重度 (CDAI 220以上450以下) のクローン病患者
- 生物学的製剤及び免疫調節剤未治療の患者
- TPMP正常の患者
- 以下の項目を少なくとも1つ満たす患者
 - ・ステロイド依存性
 - ・過去1年間に少なくとも2回以上のステロイド増量を考慮された
 - ・5-ASA製剤不応
メサラミン (2.4 g/日以上) で少なくとも4週間治療しても効果不十分
 - ・ブデソニド不応
ブデソニド (6 mg/日以上) で少なくとも4週間治療しても効果不十分

試験デザイン



治療開始前に3群に無作為割付を行った。