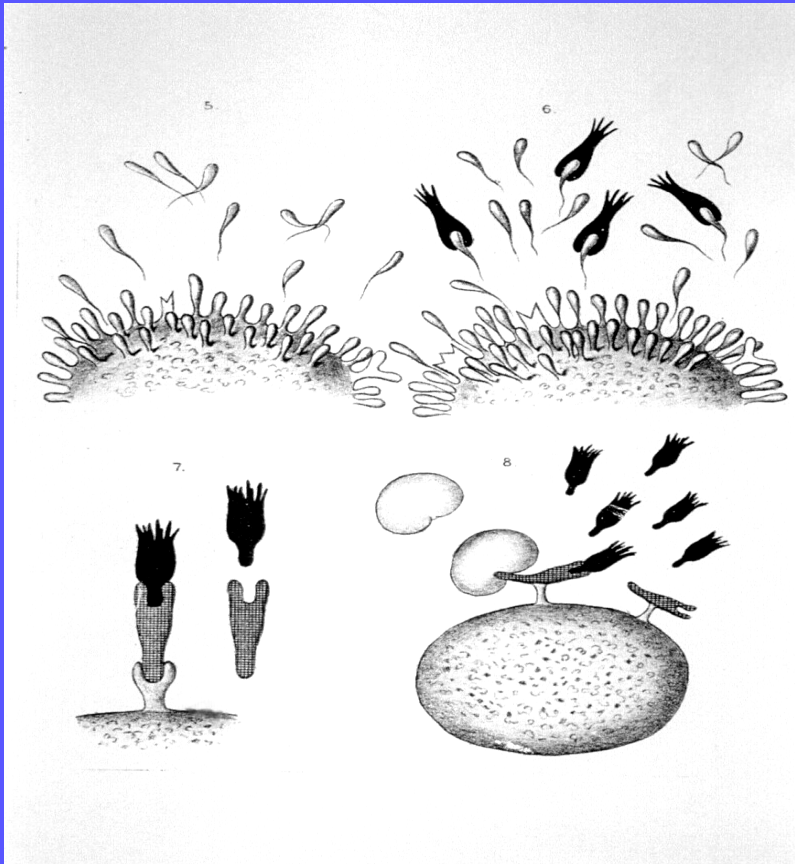


MONOCLONAL ANTIBODIES AS TREATMENT FOR B-CELL LYMPHOMAS



Ama Rohatiner, INCTR(UK)
St. Bartholomew's Hospital,
London

Ehrlich P : 'On immunity with special reference to cell life.'

Proc. R. Soc. Lond (Biol) 1890

MONOCLONAL ANTIBODIES AS TREATMENT FOR B-CELL LYMPHOMAS

1) ANTI-CD20 : RITUXIMAB/MABTHERA

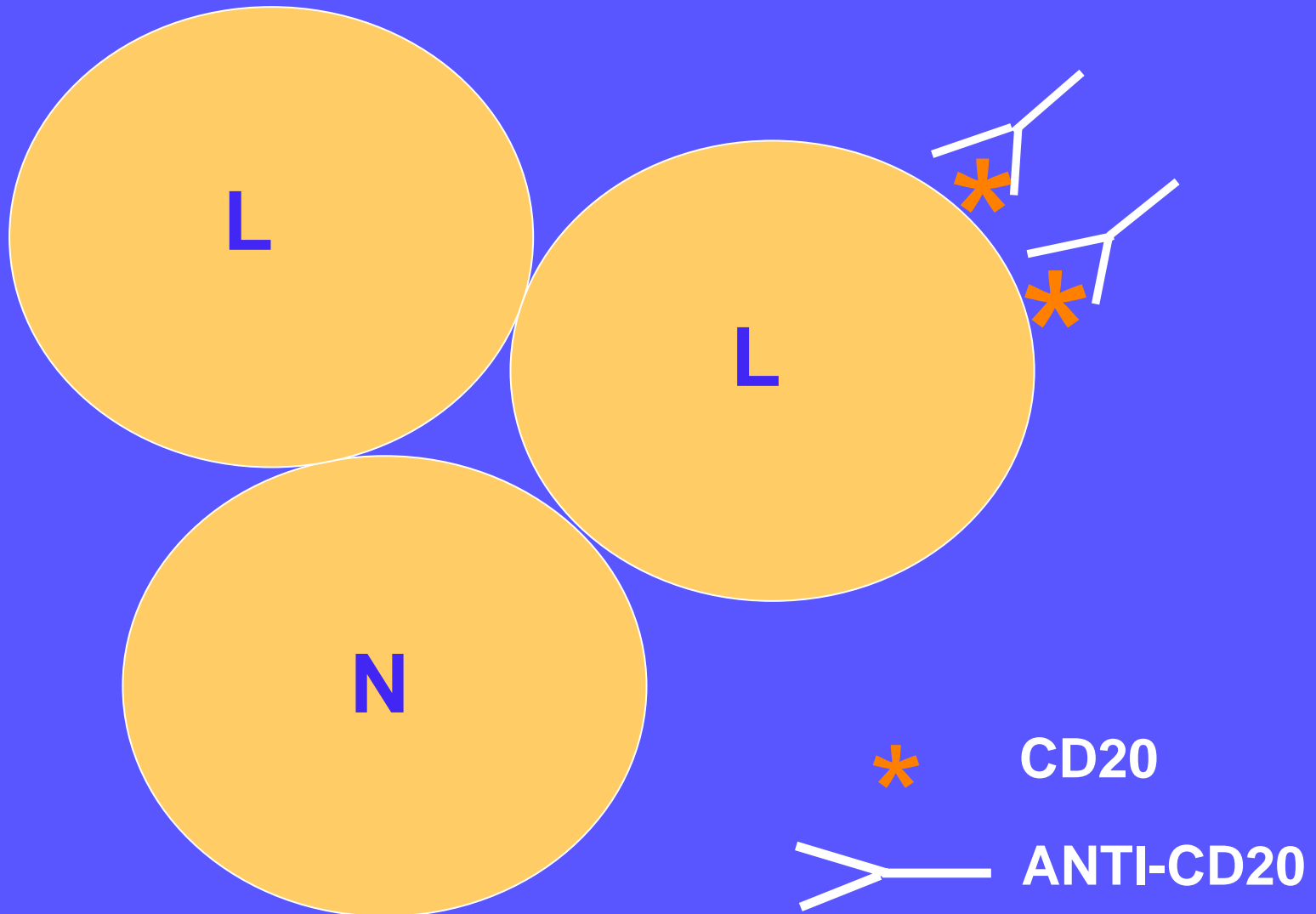
2) RADIOACTIVE ANTIBODIES(RADIOIMMUNOTHERAPY)

- ¹³¹I ANTI - CD20 : BEXXAR

- ⁹⁰Y ANTI - CD20 : ZEVALIN

3) ANTI - CD22 + CALICHEAMYCIN

MONOCLONAL ANTIBODIES AS TREATMENT FOR B-CELL LYMPHOMAS: RITUXIMAB



MONOCLONAL ANTIBODIES AS TREATMENT FOR B-CELL LYMPHOMAS:RITUXIMAB

DOSE: EMPIRICAL.....

375mg/m² X 4 WEEKLY INFUSIONS

- based on limited availability of drug for 1st Phase II study
- do not need this much to saturate binding sites

SCHEDULE: QUESTIONABLE.....

- ?EVERY 2 - 3 MONTHS

Berinstein et al, Ann. Oncol.1998, Gordan et al, JCO:2005

CLINICAL TOXICITY

- USUALLY MINIMAL THOUGH ANAPHYLAXIS CAN OCCUR

MONOCLONAL ANTIBODIES AS TREATMENT FOR B-CELL LYMPHOMAS:RITUXIMAB

COST (TO N.H.S. in U.K.)* for a PERSON 1.8 sq.m

4 INFUSIONS = £5,776

*APPROVED BY 'NICE' AS PART OF 1st LINE TREATMENT
FOR FOLLICULAR and DIFFUSE LARGE B-CELL
LYMPHOMAS

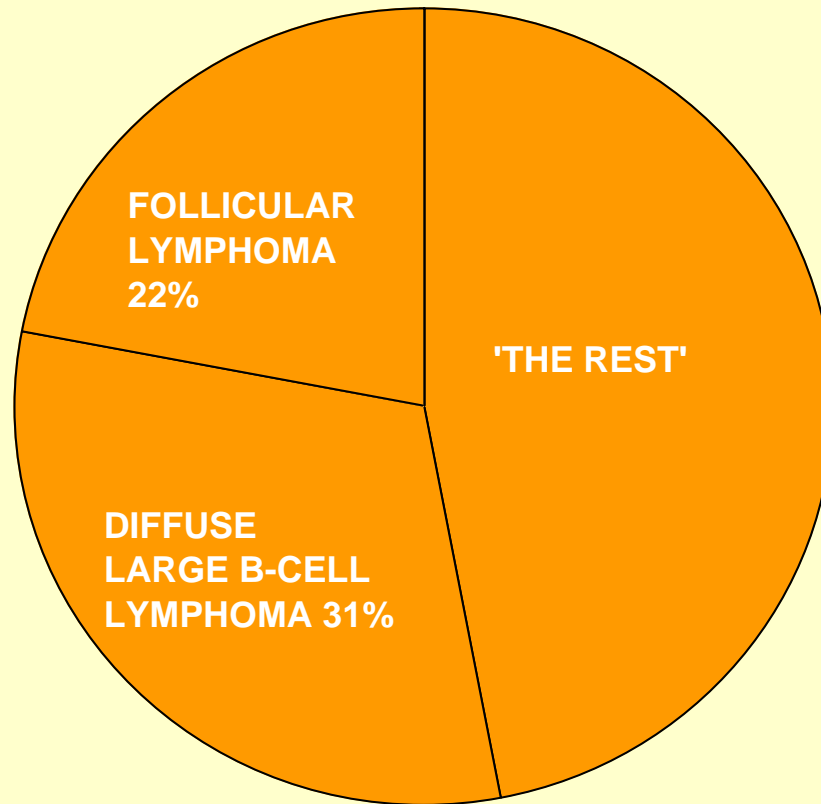
MONOCLONAL ANTIBODIES AS TREATMENT FOR B-CELL LYMPHOMAS:RITUXIMAB

(ALONE) - RESPONSE TO CHEMOTHERAPY BETTER

WITH CHEMOTHERAPY

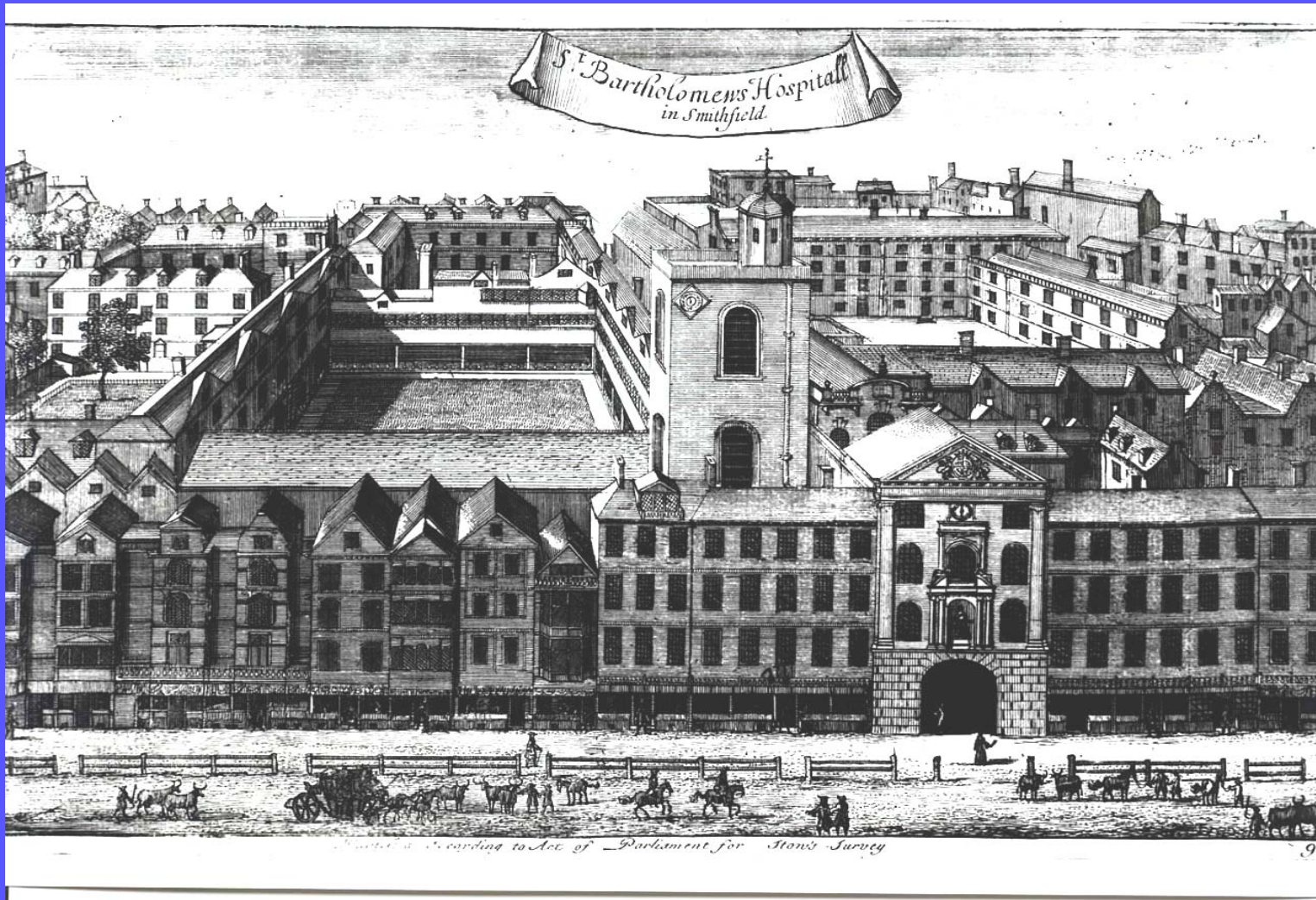
AS MAINTENANCE THERAPY

NON-HODGKIN'S LYMPHOMAS



CD20+

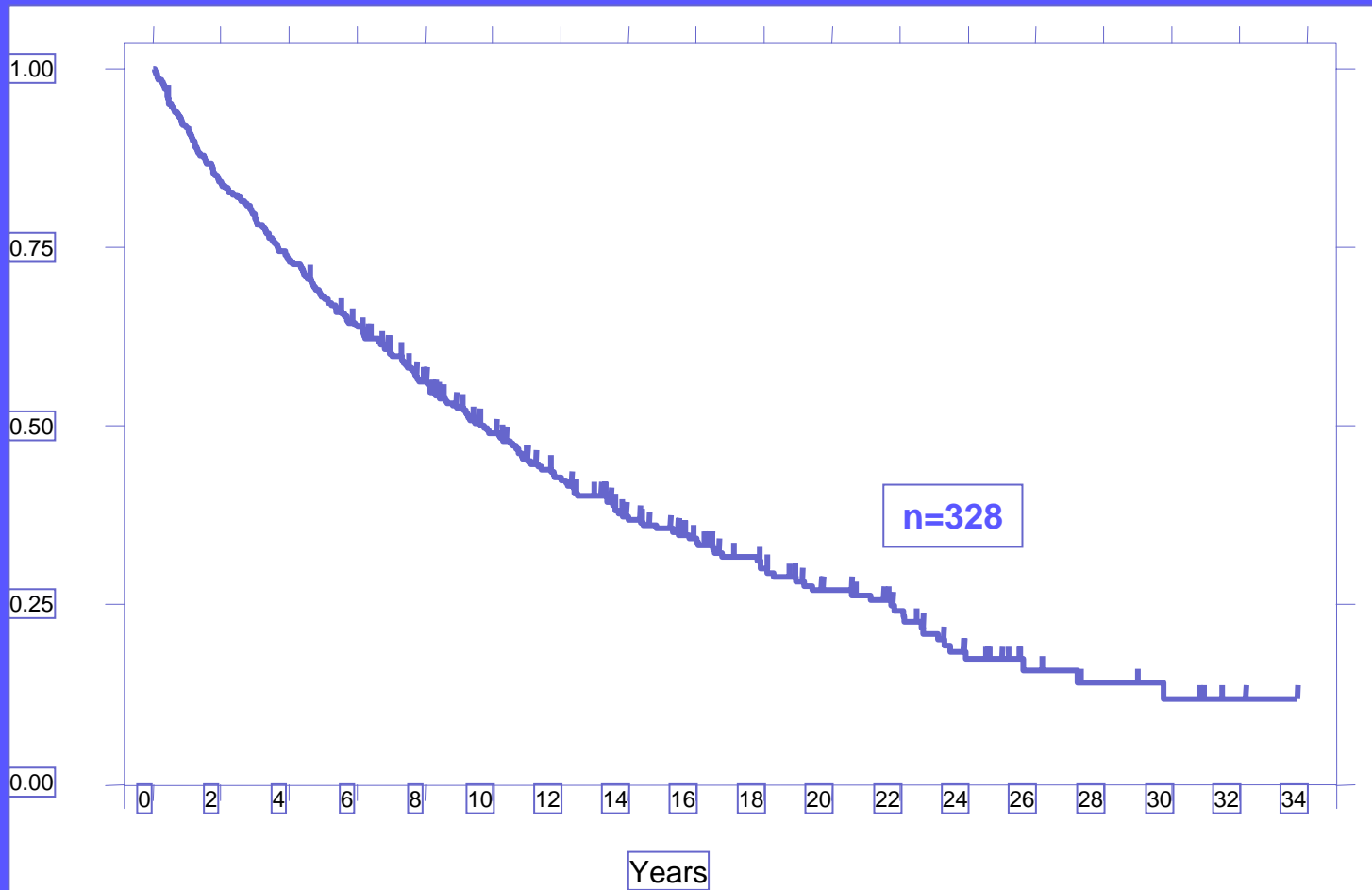
International Classification Project, JCO 1998, 16, 2782



ST. BARTHOLOMEW'S HOSPITAL, LONDON
- founded for the 'sick poor' of London, 1132 AD

FOLLICULAR LYMPHOMA: SURVIVAL

1972 - 1999



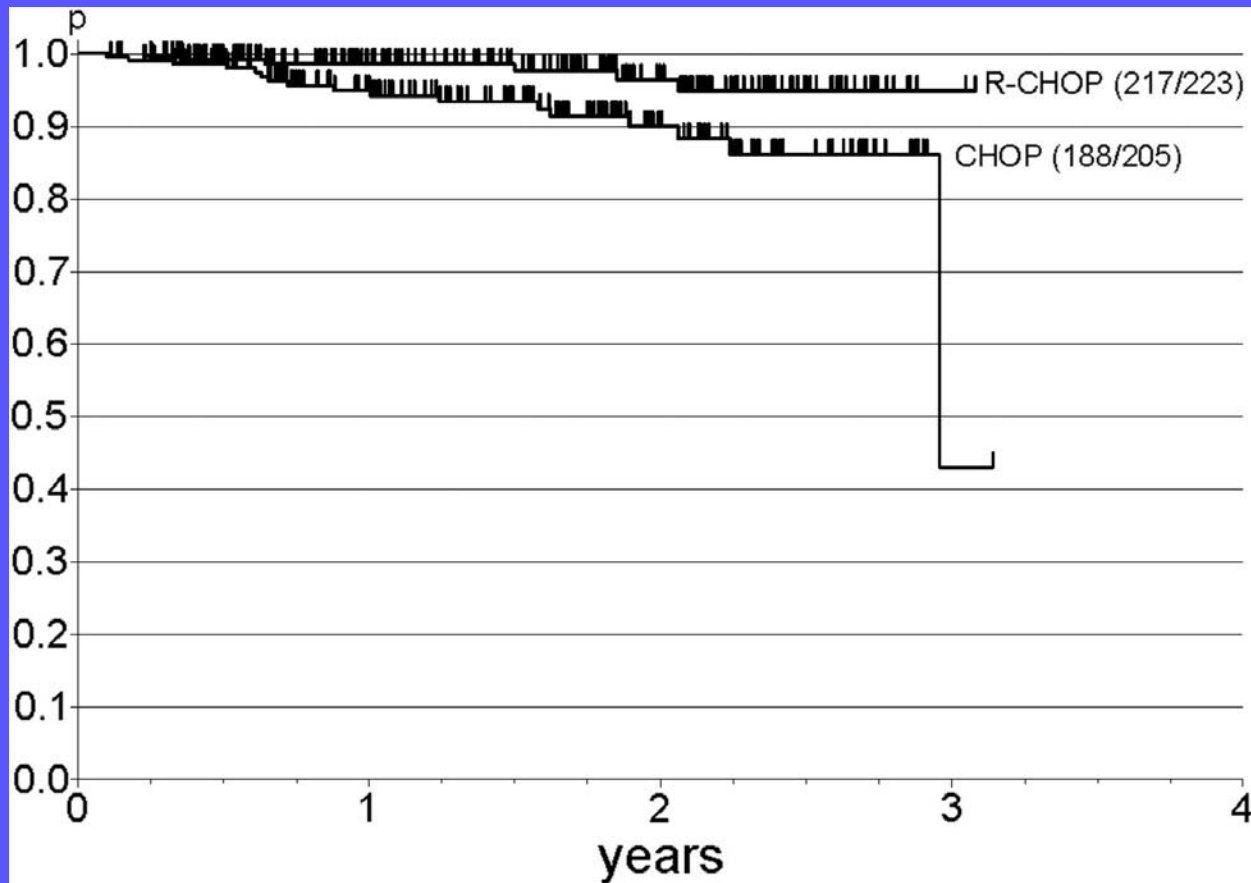
MONOCLONAL ANTIBODIES AS TREATMENT FOR B-CELL LYMPHOMAS

FOLLICULAR LYMPHOMA: CT + RITUXIMAB vs CT

TREATMENT	RESPONSE RATE	STUDY
AT RECURRENCE FCM+R vs FCM	RR 94% vs 71% CR 39% vs 23% * SURVIVAL DIFFERENCE	Dreyling et al 2005
NEWLY DIAGNOSED CVP+R vs CVP	RR 81% vs 57% TTP: 30 vs 15m	Marcus et al 2005
CHOP+R vs CHOP	TTF: NYR vs 2.6y * SURVIVAL DIFFERENCE	Hiddeman et al 2005
MCP+R vs MCP	RR, CR rate, PFS * SURVIVAL DIFFERENCE	Herold et al 2005

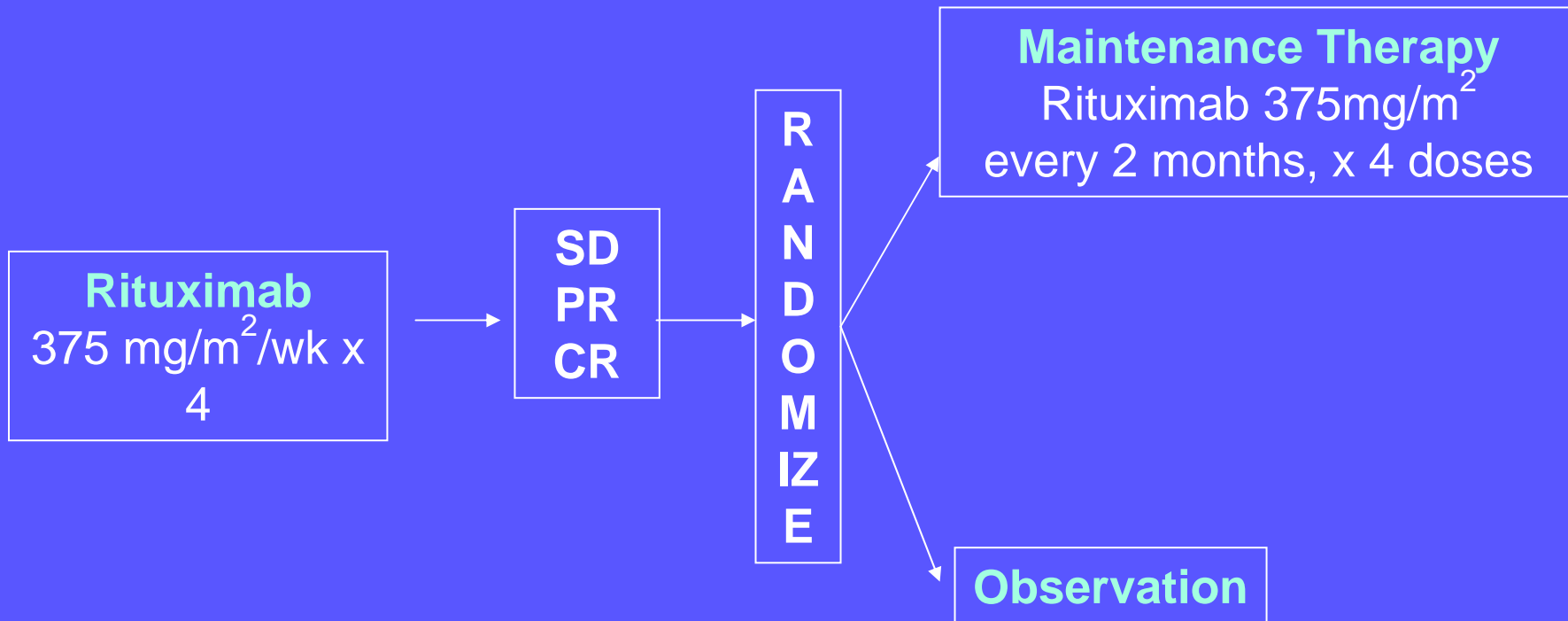
FOLLICULAR LYMPHOMA

CHOP vs CHOP+ RITUXIMAB: SURVIVAL

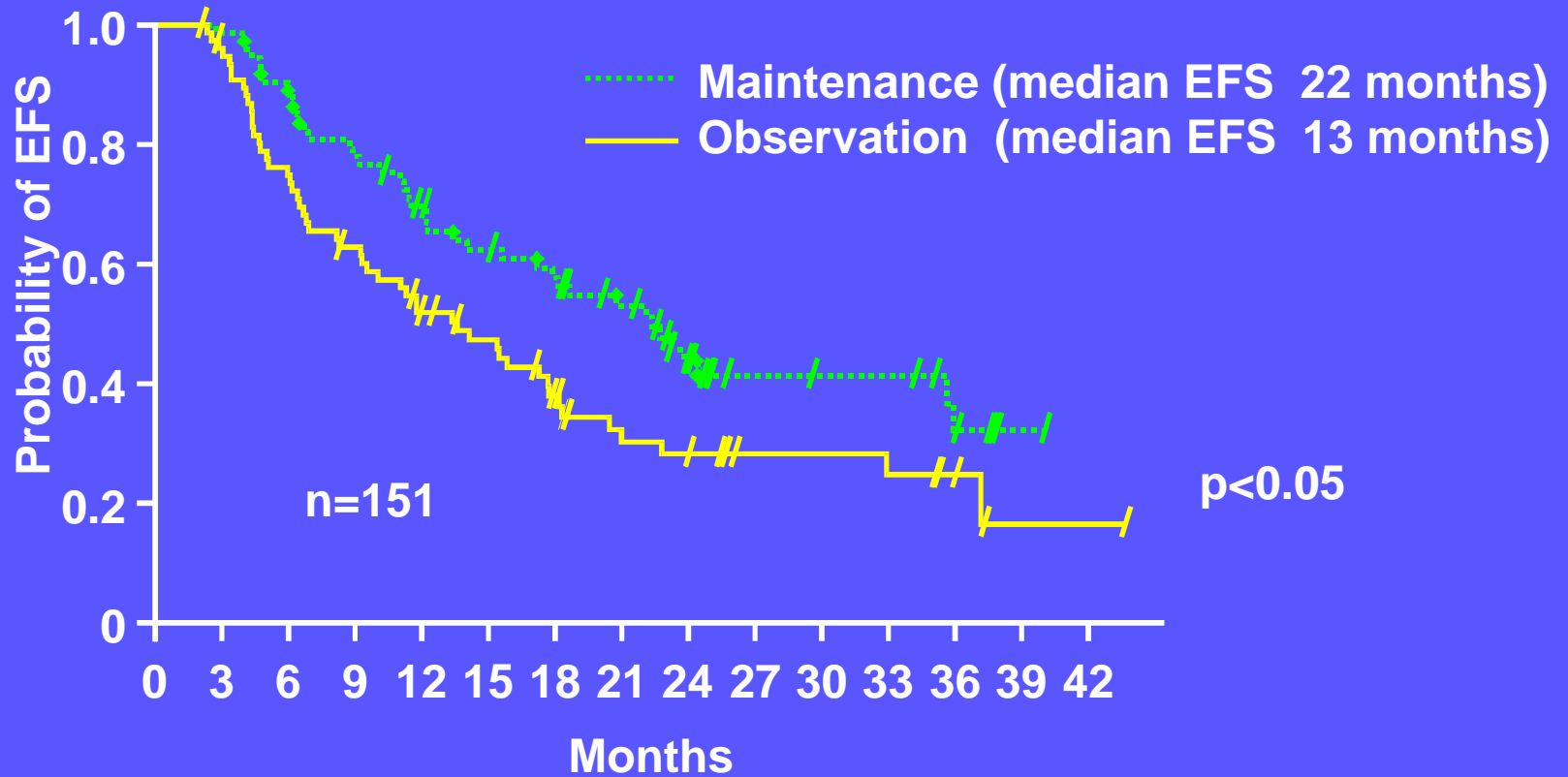


Hiddemann, et al. Blood 2005, 106:3725-3732

MAINTENANCE THERAPY FOR FOLLICULAR LYMPHOMA RITUXIMAB AT RECURRENCE → MAINTENANCE



MAINTENANCE THERAPY FOR FOLLICULAR LYMPHOMA



FOLLICULAR LYMPHOMA

RITUXIMAB AFTER CT + RITUXIMAB AS INITIAL THERAPY

CVP + R x 8

or

CHOP + R x 6

or

FCM + R x 6

or

MCP + R x 6



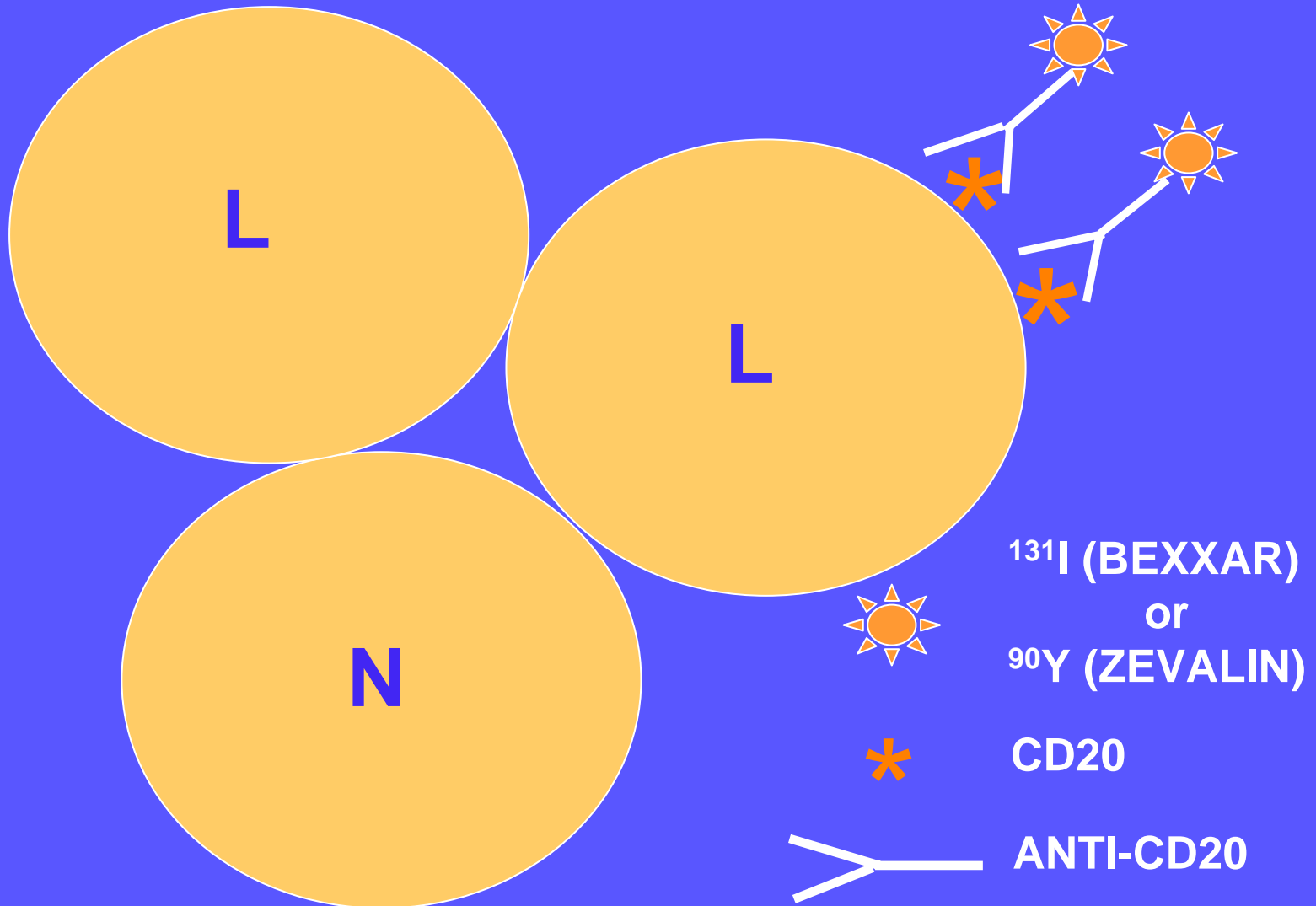
R

Maint. Rituximab
375mg/m² every
2m for 2 years

No further treatment

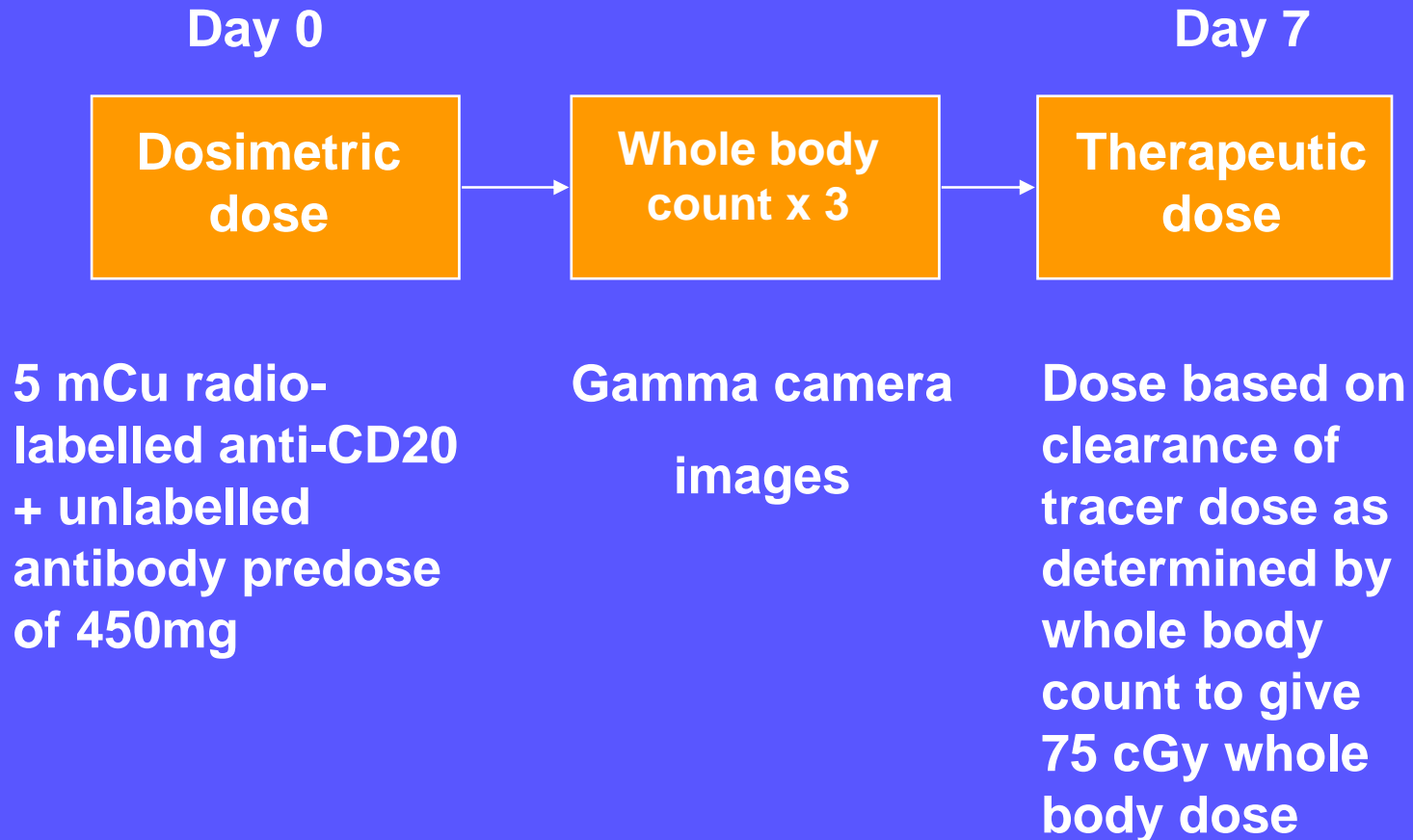
'PRIMA' STUDY

RADIOACTIVE ANTIBODIES AS TREATMENT FOR B-CELL LYMPHOMAS



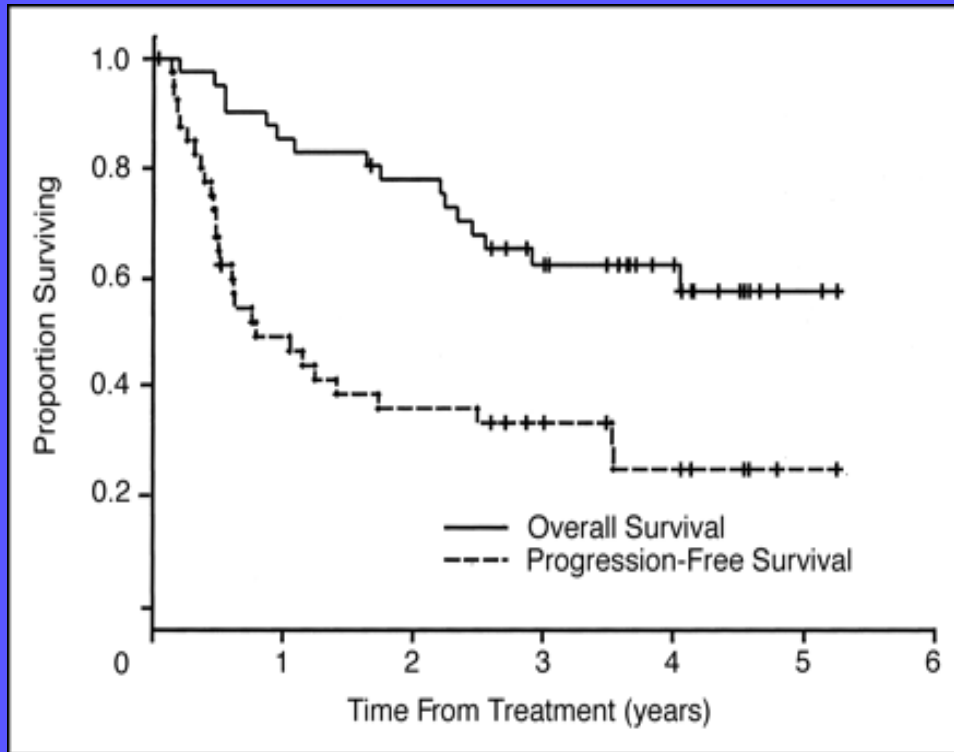
MONOCLONAL ANTIBODIES FOR B-CELL LYMPHOMA

RADIOLABELLED ANTIBODIES : BEXXAR



FOLLICULAR LYMPHOMA

¹³¹I ANTI-CD20 : PHASE II STUDY, U.K.



SBH and CHRISTIE HOSPITALS

88 PTS at 1st.or 2nd. RECURRENCE

RR: 80 % in FOLLICULAR LYMPHOMA

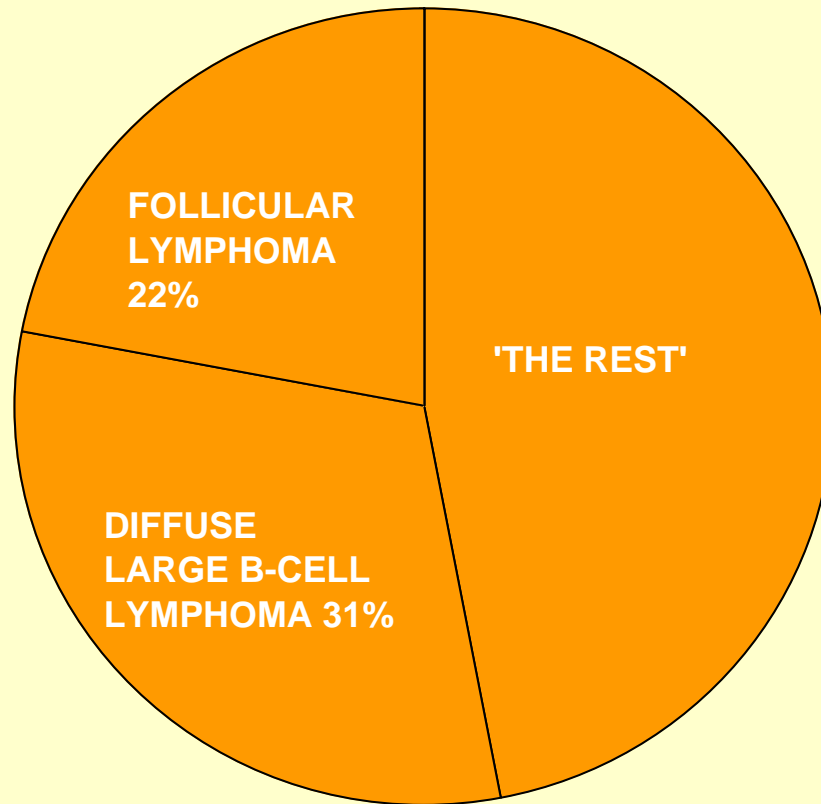
EFFECTIVE in PTS. WHO HAD PREVIOUSLY RECEIVED HDT OR RITUXIMAB

FOLLICULAR LYMPHOMA: RADIOACTIVE ANTIBODIES WHAT CAN WE CONCLUDE?

**GOOD TREATMENTS - COMPLICATED
ZEVALIN GIVEN AS AN OUT-PATIENT**

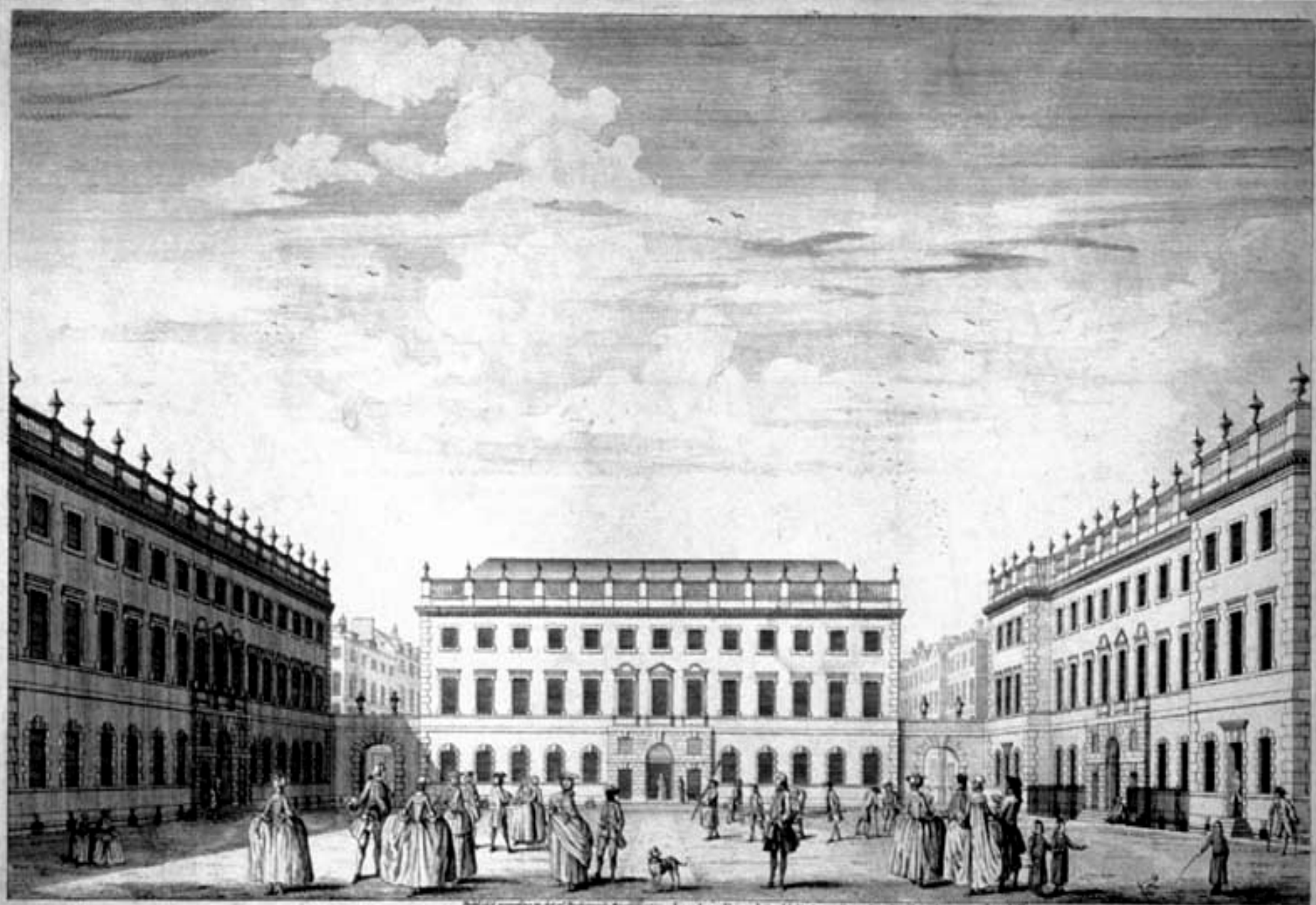
**PROBLEM: BEXXAR NOT AVAILABLE
ZEVALIN:£10,581 - PRICE PRECLUDES
MOST PEOPLE FROM RECEIVING IT**

NON-HODGKIN'S LYMPHOMAS



CD20+

International Classification Project, JCO 1998, 16, 2782



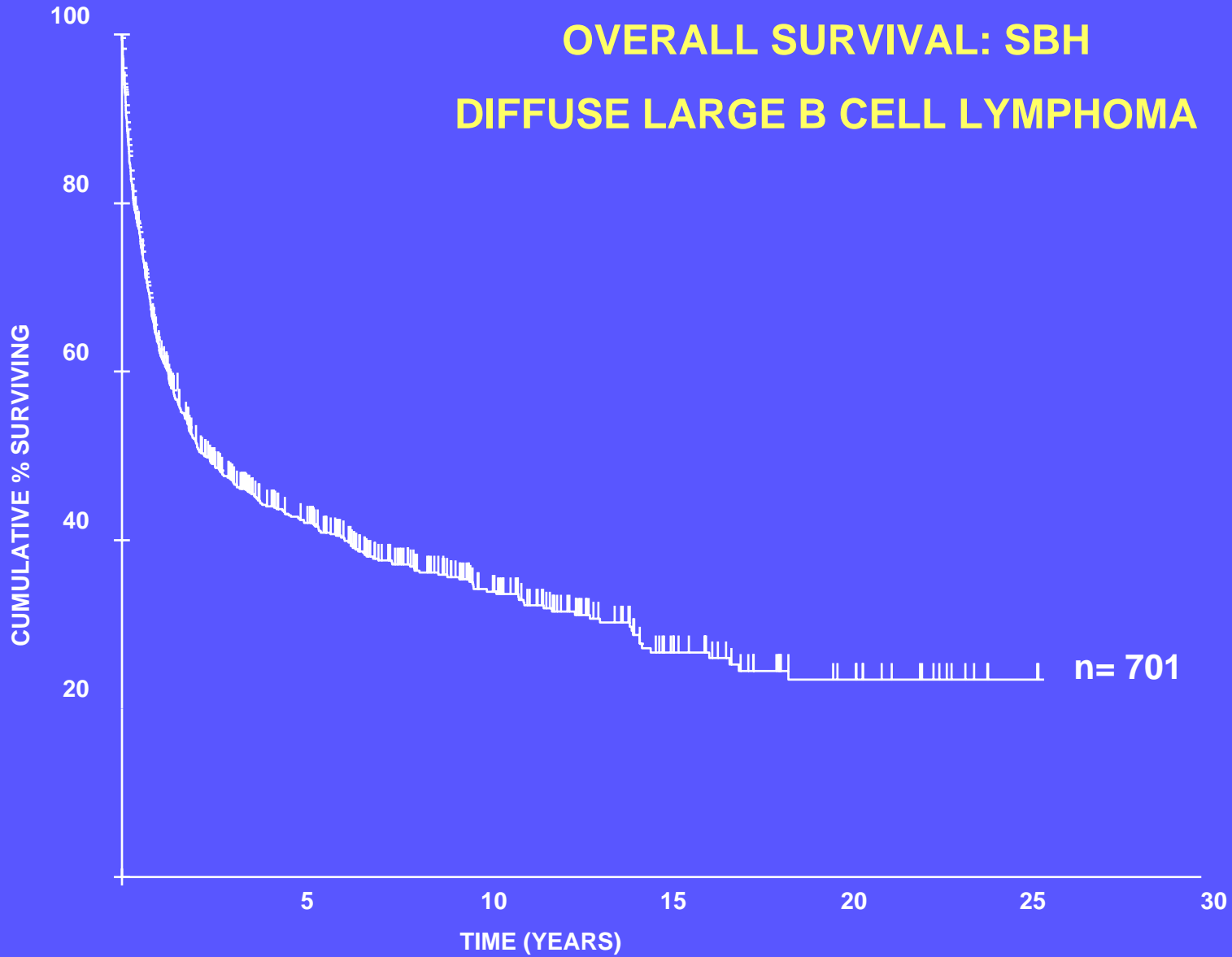
Engraved by Robert Smith, & Del. & Engraved by Wm. Woodcock, for John Wages, and on June 9 1770. From the best Prints of this Fabric now kept.

London. Printed by H. Parker, Opposite Bachelors Lane in Cornhill.

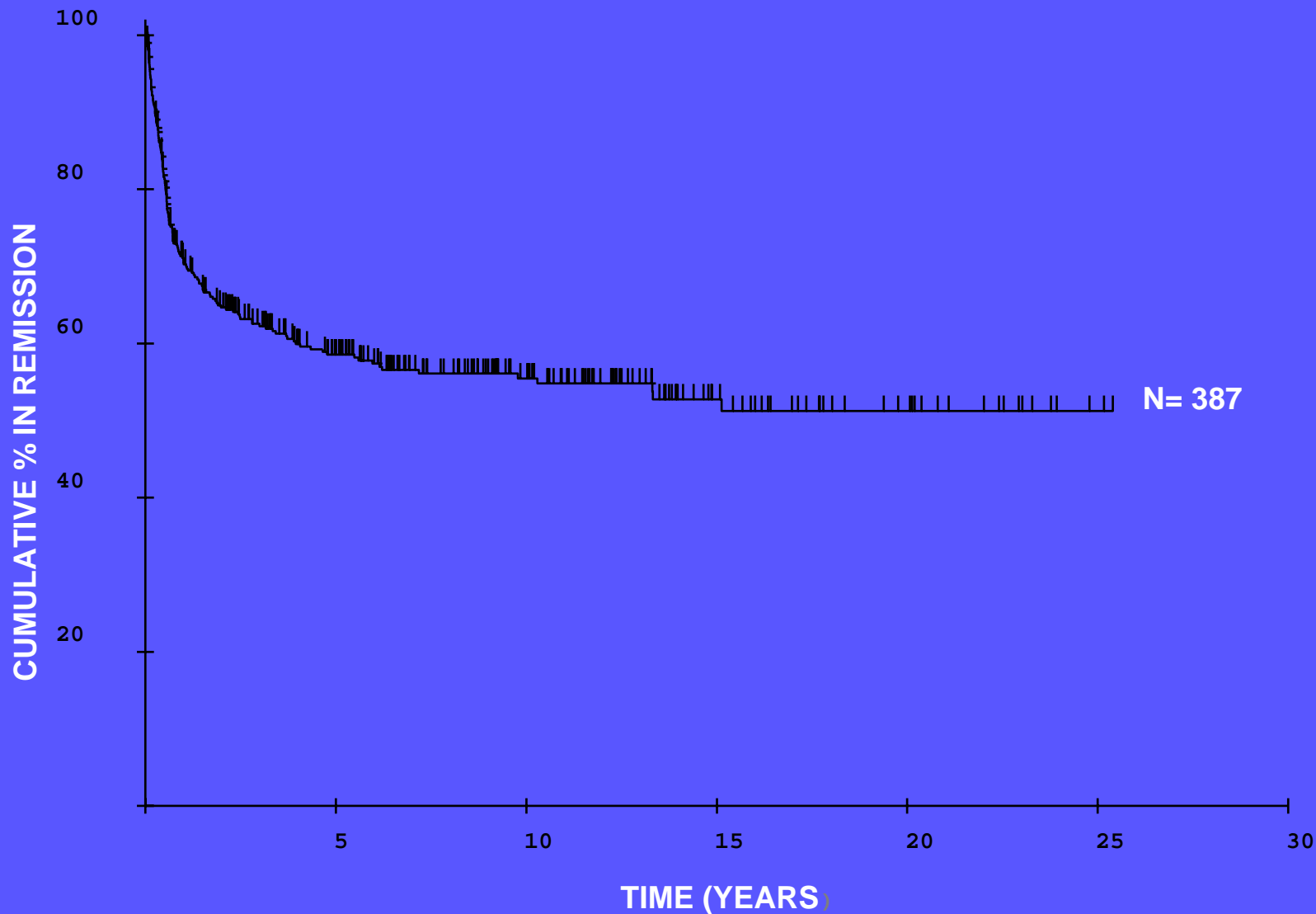
Vue de l'Hopital de S. Barthelemi du Cote de l'Orient.

La Premiere Partie de cette Religion est par le Roy de France en 1220. Elle fut rebâtie par Philippe le Bel en 1280. Elle fut rebâtie par Louis XII. et achevée par Louis XIII.

OVERALL SURVIVAL: SBH DIFFUSE LARGE B CELL LYMPHOMA



DIFFUSE LARGE B-CELL LYMPHOMA: REMISSION DURATION



MONOCLONAL ANTIBODIES AS TREATMENT FOR B-CELL LYMPHOMAS : DLBC LYMPHOMA

OLDER PATIENTS: 'CHOP' + RITUXIMAB

↑ CR RATE

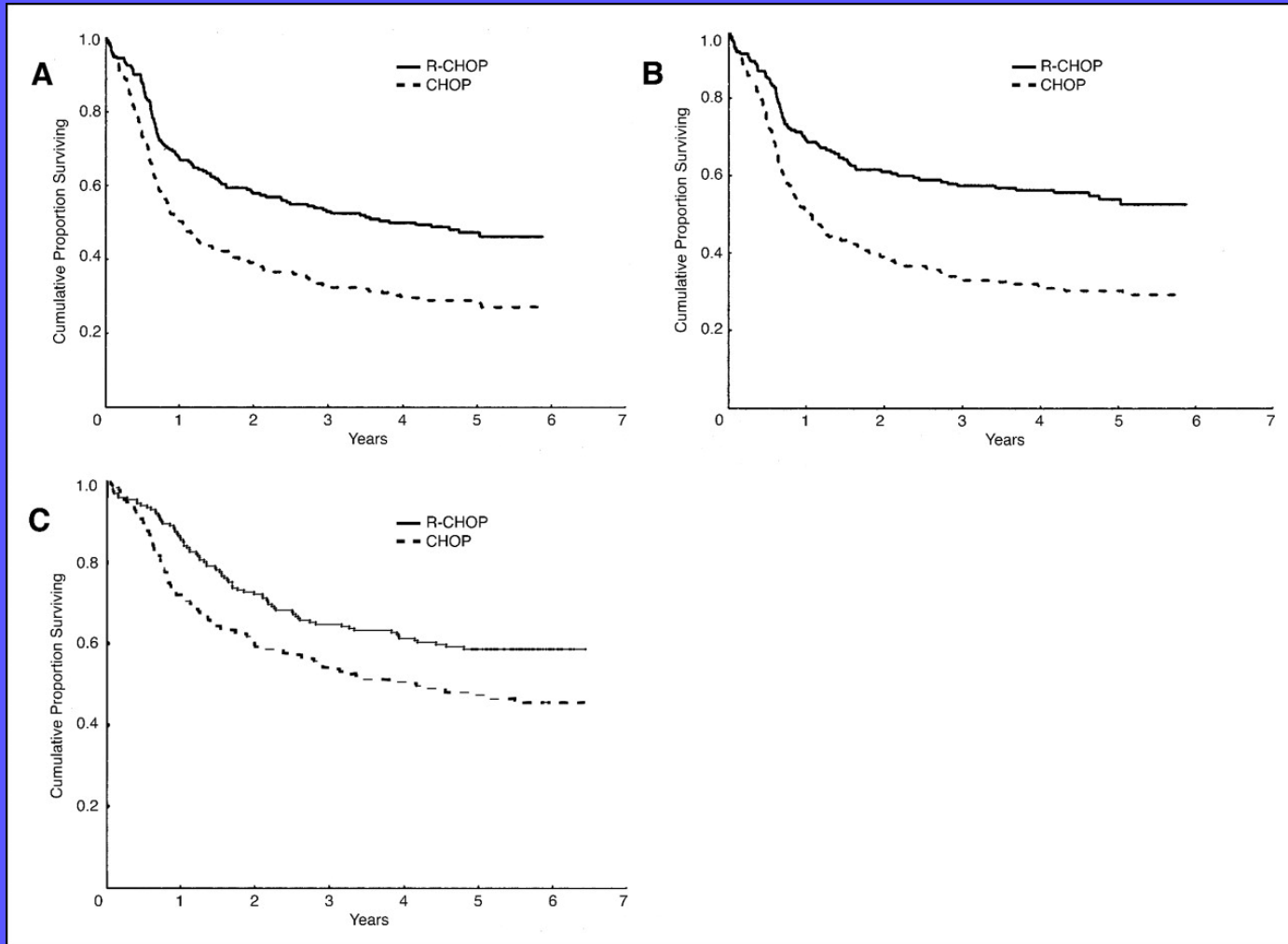
↑ EVENT-FREE SURVIVAL

↑ SURVIVAL

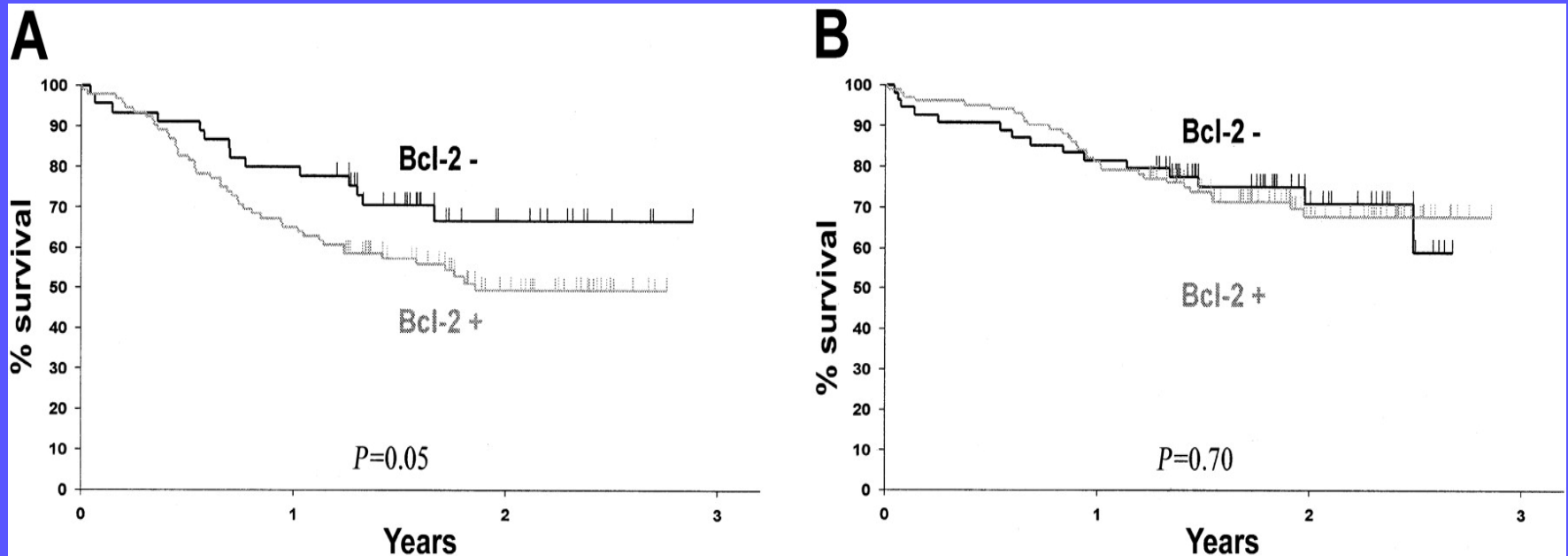
Coiffier et al, NEJM, 346:235,2002

DLBC LYMPHOMA: CHOP + RITUXIMAB

(A) Event-free survival, (B) progression-free survival, and (C) overall survival



MONOCLONAL ANTIBODIES AS TREATMENT FOR B-CELL LYMPHOMAS : DLBC LYMPHOMA

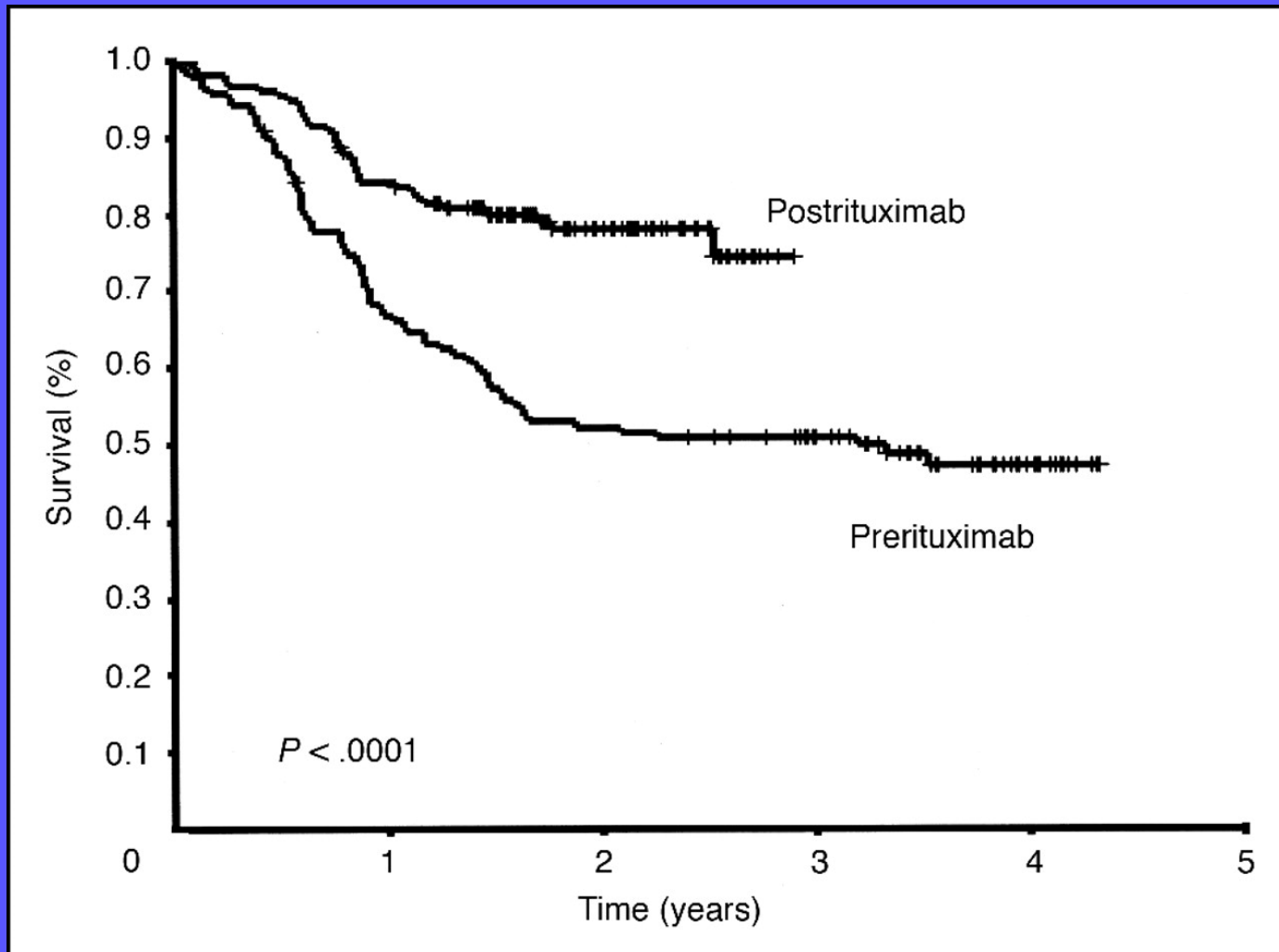


SURVIVAL ACCORDING TO BCL-2 PROTEIN EXPRESSION

WORSE PROGNOSIS ASSTD. WITH Bcl-2+ ABROGATED BY ADDITION OF RITUXIMAB

Mounier, N. et al. Blood 2003;101:4279-4284

DLBC LYMPHOMA: CANADIAN RETROSPECTIVE ANALYSIS - OVERALL SURVIVAL BY TREATMENT ERA



DIFFUSE LARGE B-CELL LYMPHOMA
ADDING RITUXIMAB:WHAT CAN WE CONCLUDE?

IMPROVES OUTCOME

PROBLEM: PRICE PRECLUDES

MOST PEOPLE FROM RECEIVING IT

DIFFUSE LARGE B-CELL LYMPHOMA ADDING RITUXIMAB:SOLUTIONS?

**1) PROPOSAL FOR INTERNATIONAL RANDOMISED
PHASE III STUDY (INCTR)**

+

'MOLECULAR' ADD-ON STUDIES

2) ASK ROCHE TO EMULATE NOVARTIS (CML)