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MD Anderson Cancer Center
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Phase II Open Label Trial of Brentuximab Vedotin (SGN-35) for CD30+ Lymphoproliferative Disorders and CD30+ Mycosis Fungoides

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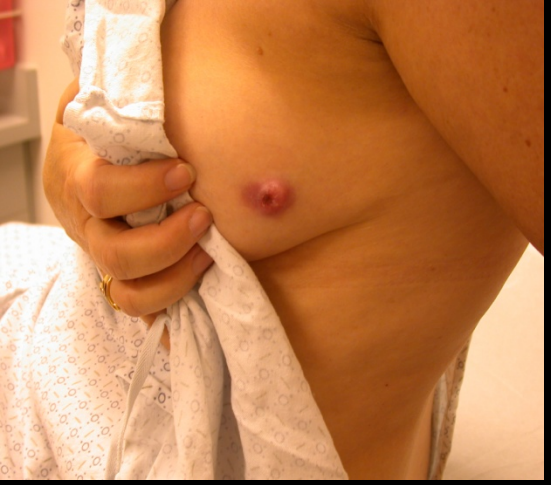
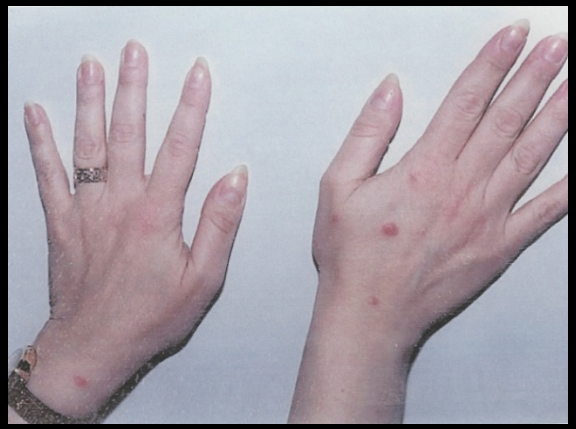
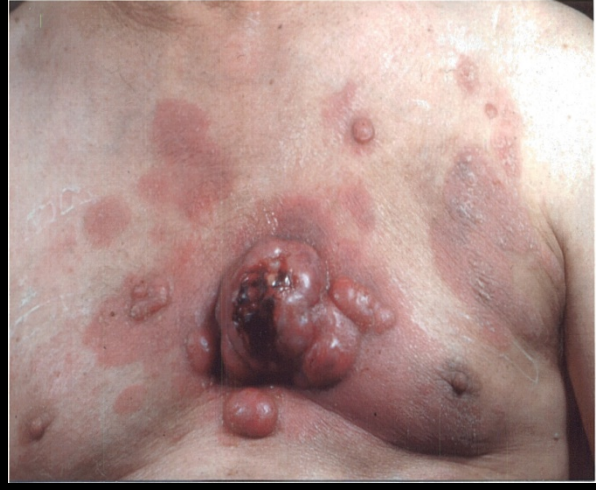


Lymphomatoid Papulosis





Primary cutaneous Anaplastic T-cell Lymphoma

Transformed CD30+ Mycosis Fungoides

CD30+ Cutaneous T cell lymphomas

Lymphomatoid Papulosis
LyP

Primary Cutaneous ALCL
c-ALCL

CD30+ Lymphoproliferative Disorders

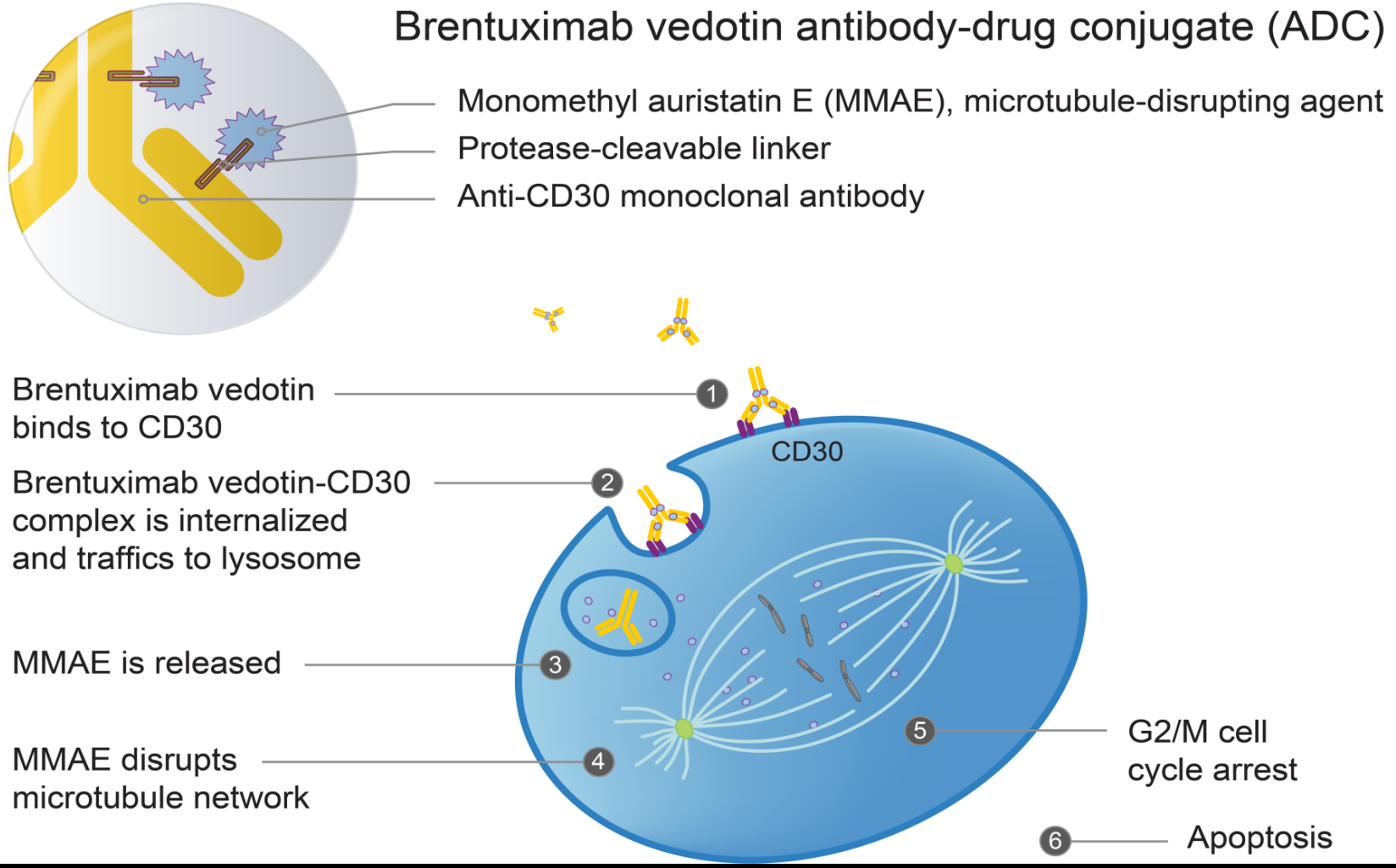
Mycosis Fungoides
MF or T-MF

Secondary Cutaneous ALCL

PTCL-NOS
HTLV-1
ATL

Hodgkin Lymphoma
HL

Brentuximab Vedotin Mechanism of Action



Trial Design

- A phase II investigator initiated open label trial was conducted to determine safety and efficacy of SGN-35 in cutaneous CD30+ lymphoproliferative disorders and CD30+ MF.

- SGN-35 (1.8 mg/kg) infused over 30 minutes
- Every 21 days x 8 or for PR up to 16 doses.
- Two doses past a complete response (CR).

Eligibility Criteria

- CD30+ skin lesions within past 3 years
- LyP: 10 lesions/month requiring systemic Rx
- pc-ACLC: recurrent or refractory tumors with regional LN allowed
- Mycosis fungoides: $\geq$ IB with $\geq$ 1 prior topical or systemic therapy and ECOG $\leq$ 2. Transformed MF allowed

Response Criteria

- Response criteria were specific for lesion type
  - LyP – 50% decrease in active lesion count
  - ALCL – tumor measurements of index lesions
  - MF – 50% reduction in mSWAT
- Quality of life assessments
  - Itch by VAS (1 to 10 severity)
  - Patient's global response

Evaluation of CD 30+ Expression

- One dermatopathologist (MT) evaluated CD30+ membrane and cytoplasmic atypical tumor lymphocytes in skin (membrane vs cytoplasm).
- Baseline biopsy from each type of clinical lesion MF + LyP or LyP + ALCL
- Interim and end of study skin biopsies for CR, PD, new lesions.
- Soluble serum CD30+ at baseline and end of study
- T cell clonality from multiple lesions in patient

Patient selection and dosing

- 56 patients consented
- 54 received at least one dose of SGN-35 1.8 mg/kg
  - Evaluable for safety
- 48 evaluable patients received > 2 doses and are evaluable for reponse completing the trial.
- 12 patients had dose reductions to 1.2 mg/kg
  - 9 for Grade 2 peripheral neuropathy
  - 1 for elevated liver function and fatigue
  - 2 for generalized arthralgias

Demographics of 48 patients (≥ 2 doses)

Age (y), median (range)	**59.5 years (31-77 years)**	
Sex	Male	26 (54%)
	Female	22 (46%)
Ethnicity	Caucasians	30 (63%)
	African American	13 (27%)
	Hispanics	5 (11%)
Diagnosis	Mycosis Fungoides	28
	ALCL	2
	LyP	9
	Lyp plus MF	7
	ALCL/LyP/MF	2

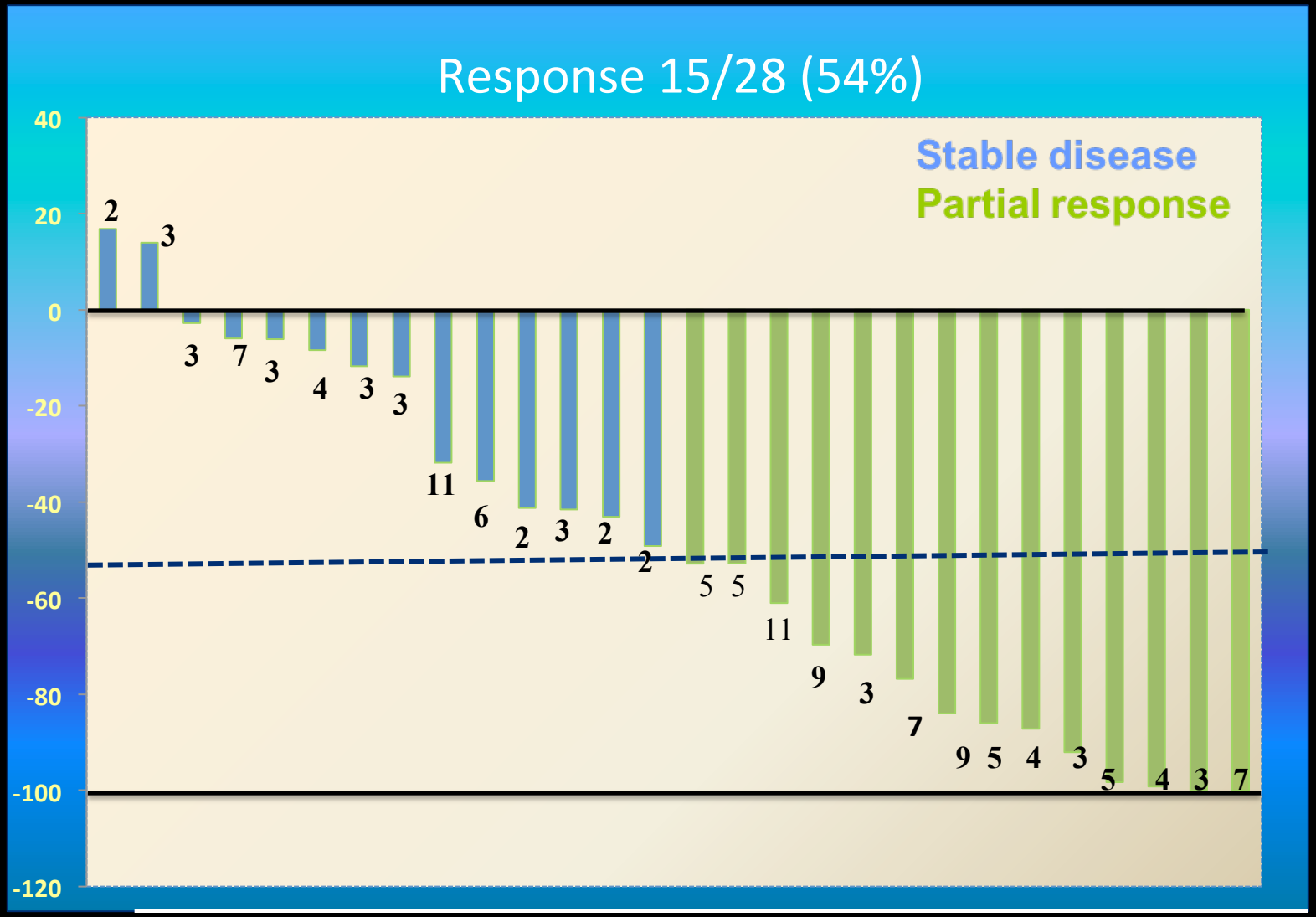
Overall Response 73% in 48 evaluable patients

Diagnosis	Total patients	Responders **73% (35/48)**		Secondary Response
MF	28	13 PR 2 CR	**54%**	x
LyP	9	5 CR 4 PR	100%	x
ALCL	2	2 CR	100%	x
LyP / MF	7	6 LyP- CR 1 LyP- PR	100%	6 MF- PR 1 MF- SD
ALCL / Lyp	1	CR	100%	1 LyP- PD
ALCL / MF	1	CR	100%	1 MF- PR

MF Overall Clinical Response 54%

Stage	Response Rate	CR	PR	SD	PD
IB (n=6)	17%	0	1	5	0
IIA (n=3)	33%	0	1	2	0
IIB (n=10)	**80%**	2	6	2	0
IIIA (n=1)	NA	0	0	0	1
IVA (n=4)	**75%**	0	3	1	0
IVB (n=4)	50%	0	2	2	0
Total = 28	54%	2	13	12	1

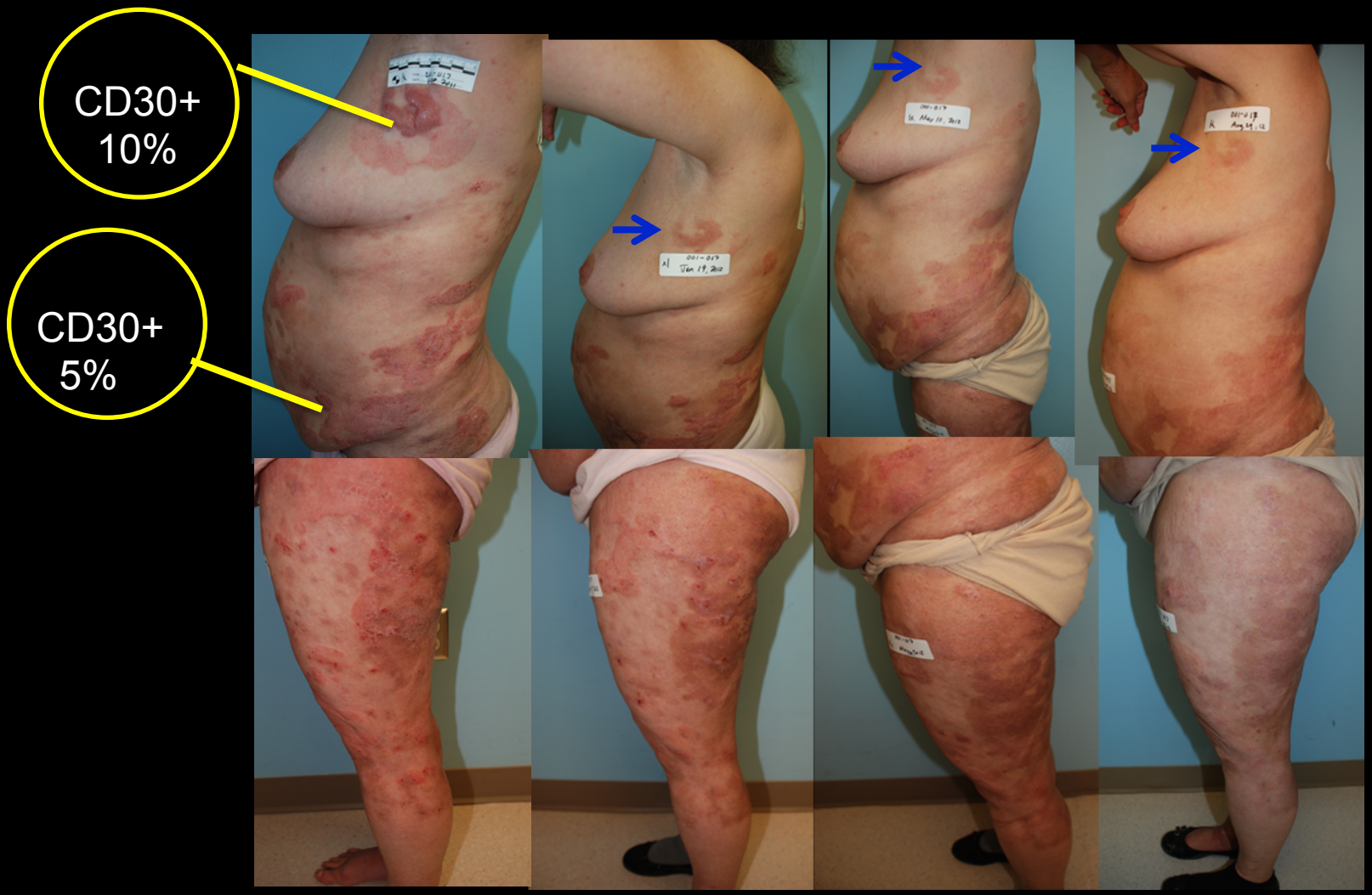
Percent Change in MF mSWAT at Best Skin Response Cycle



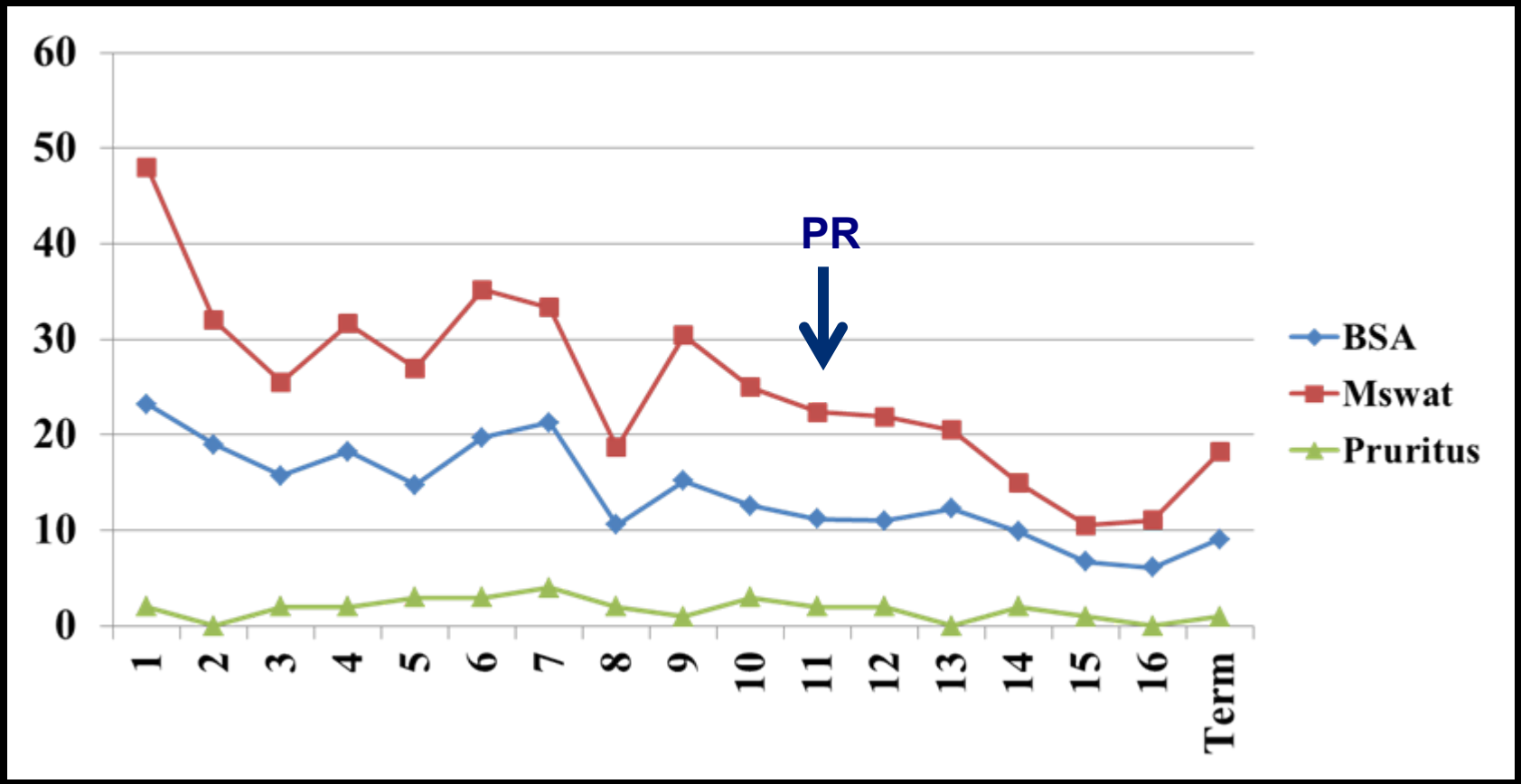
Number of Cycle at the time of Best Response

Patient 17 with CR of MF tumor C6

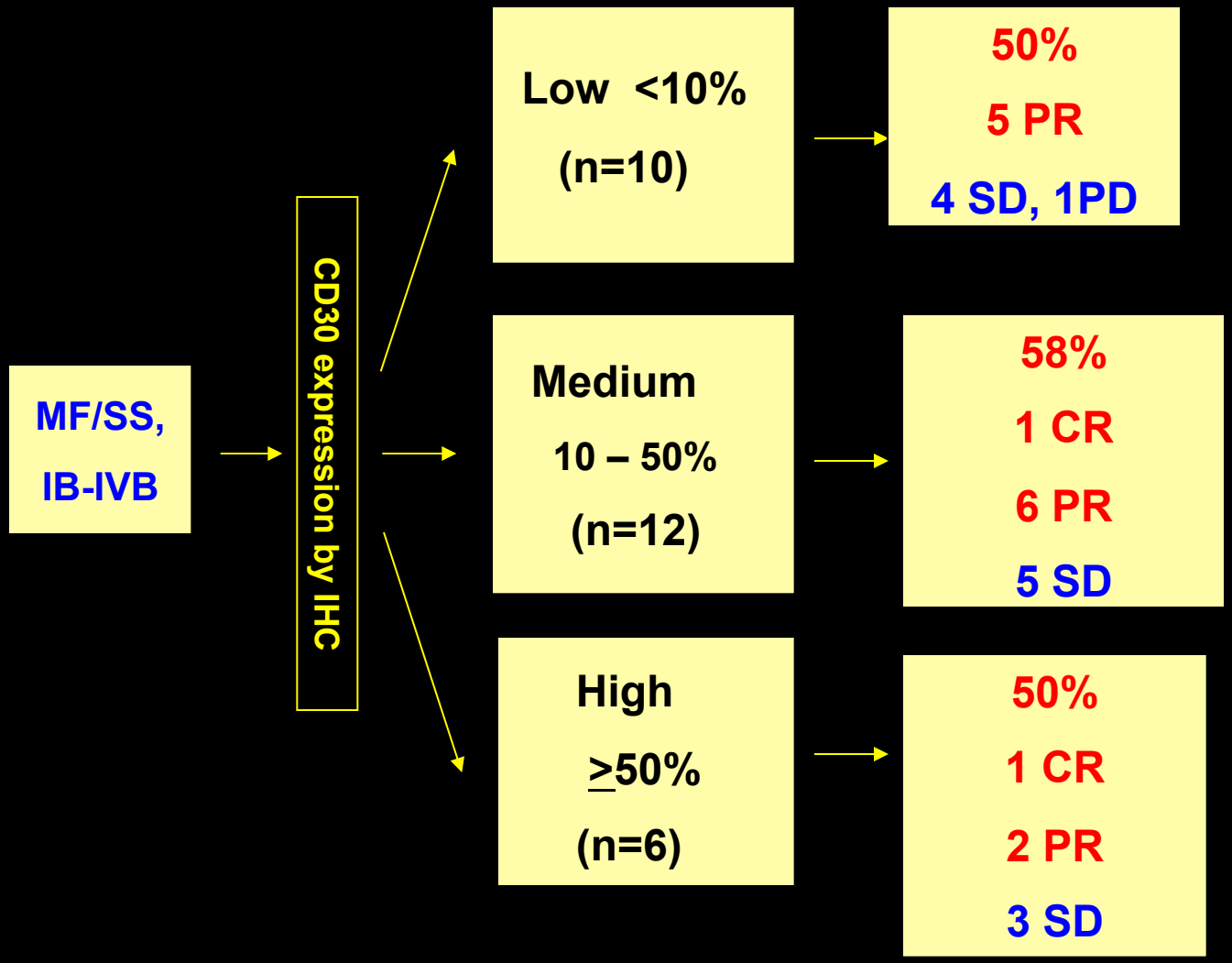
MF with PR at C11 (16 wks)



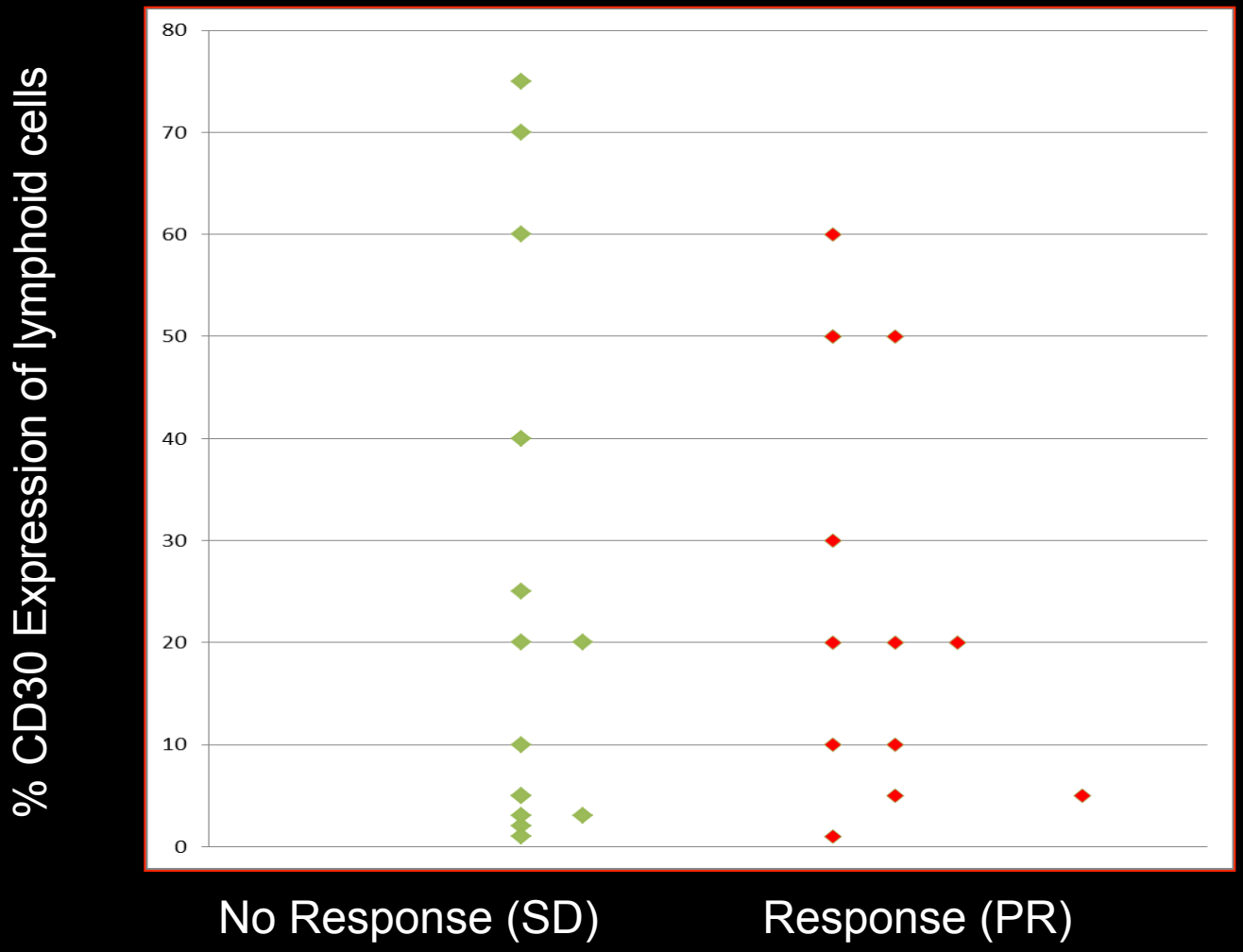
Pt 17- Response by BSA, mSWAT & Pruritus VAS



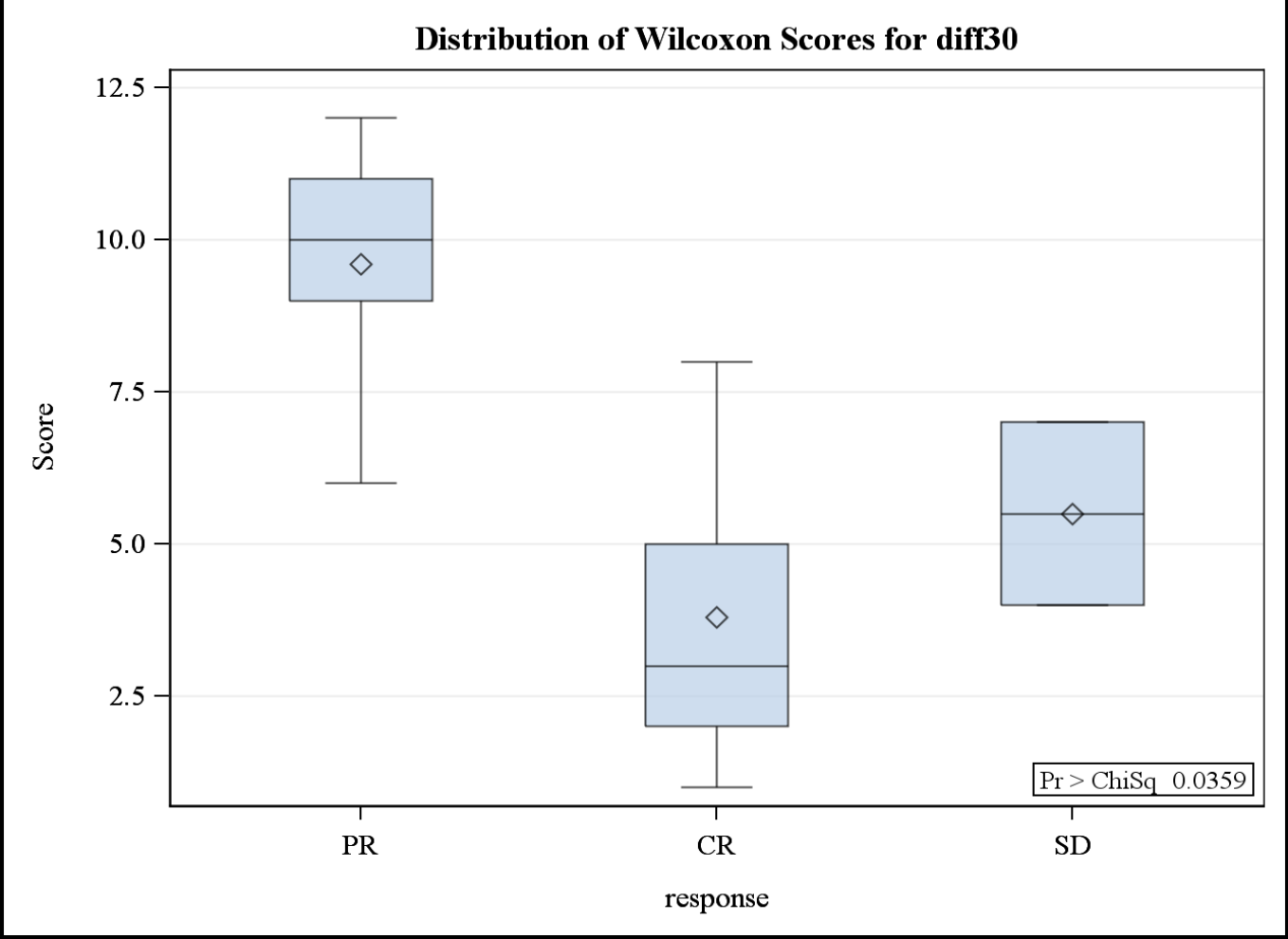
Clinical Response by Baseline CD30 Expression in 28 evaluable MF patients



No correlation between baseline CD30 and response of MF lesions

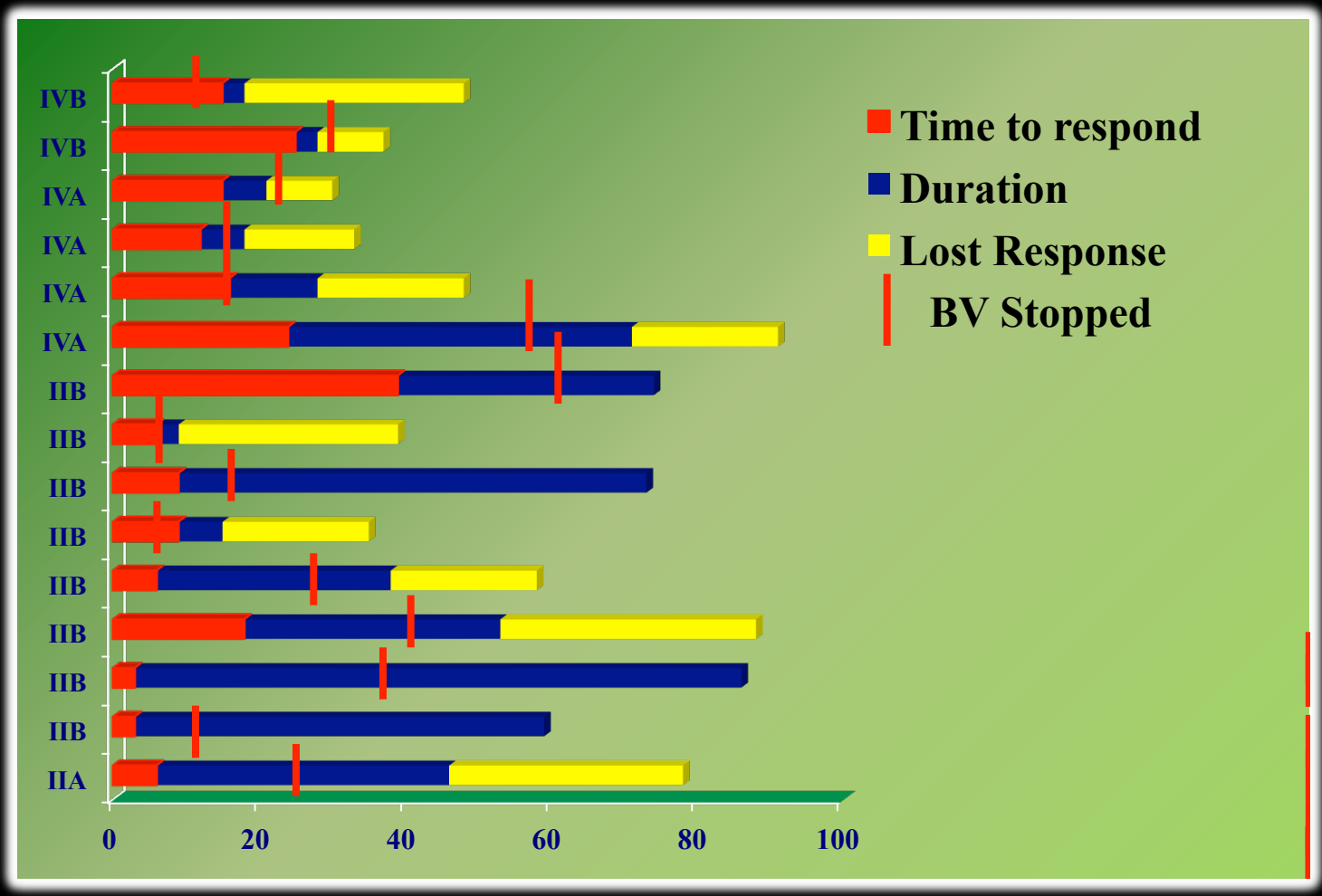


Baseline Soluble CD30 lowest in patients with CR



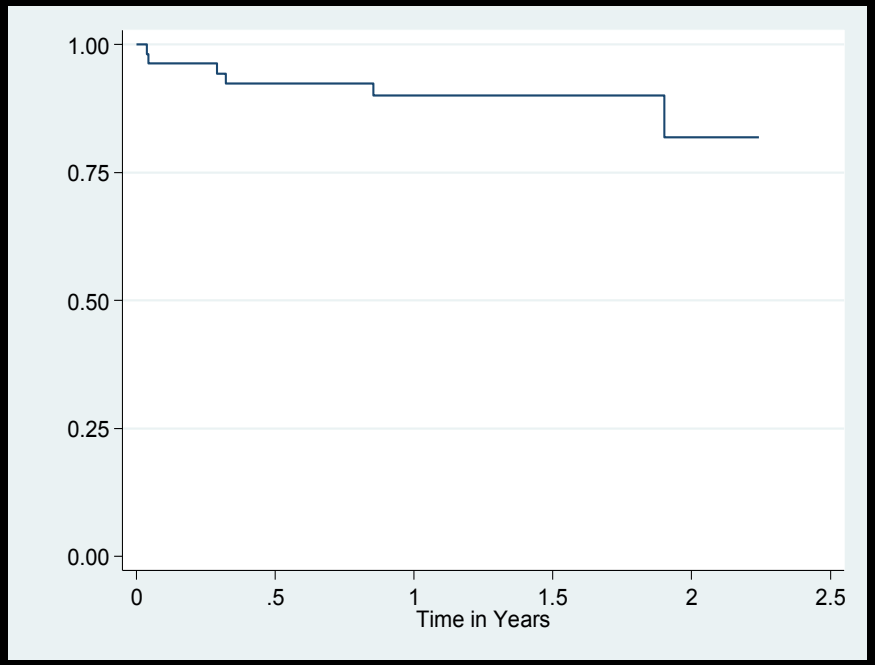
Chi square 0.03

Median Time to Response - 12 wks (3-39)
Duration of Response - 32 wks (3-93) in MF



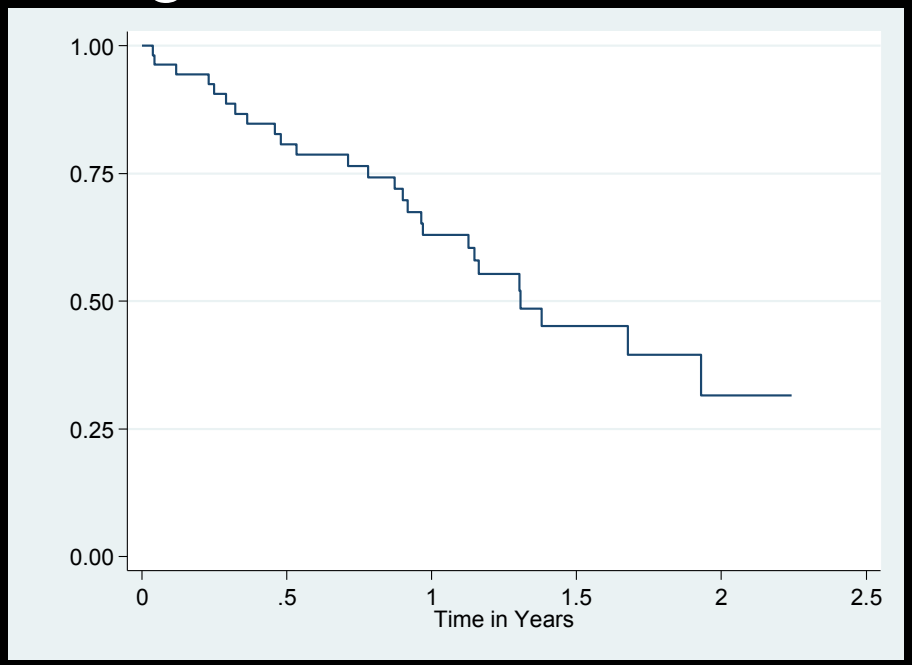
Survival from onset Brentuximab vedotin

Overall Survival



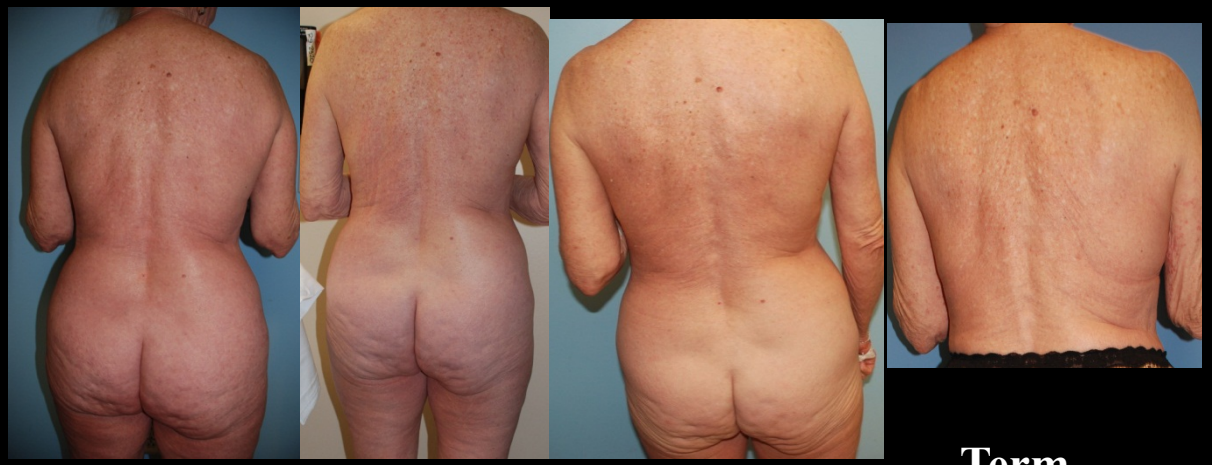
Not reached

Progression Free Survival



50% at 1.5 years

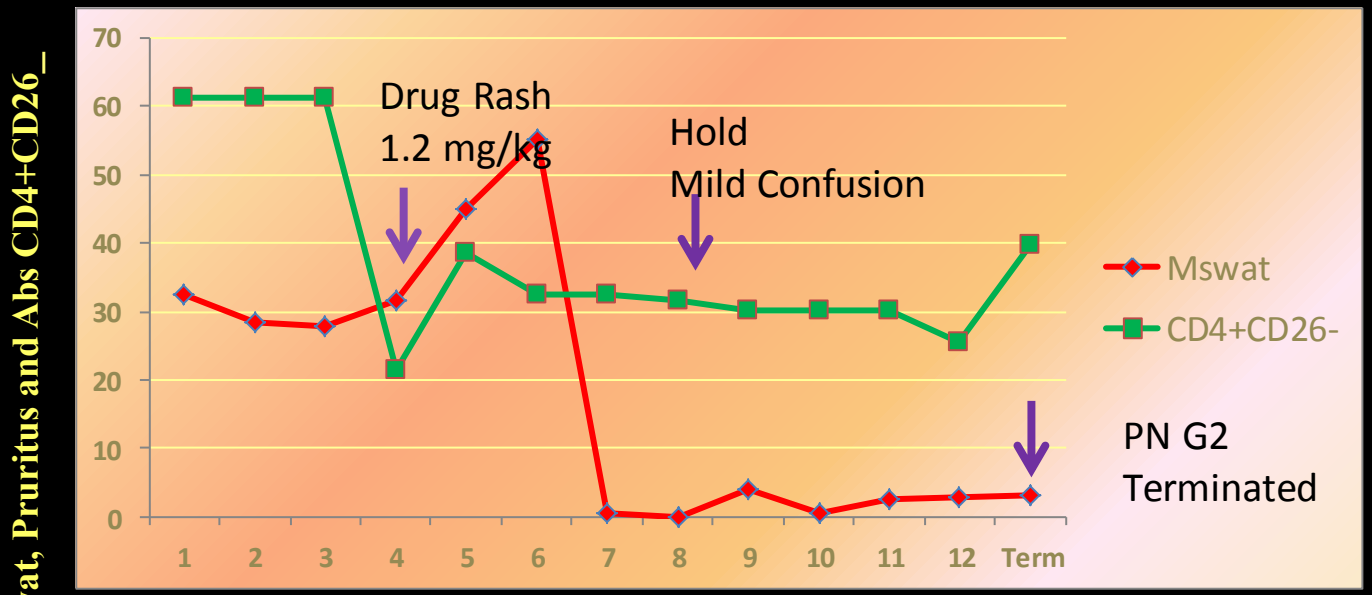
Pt 51- Near CR - Sezary IVB skin and blood



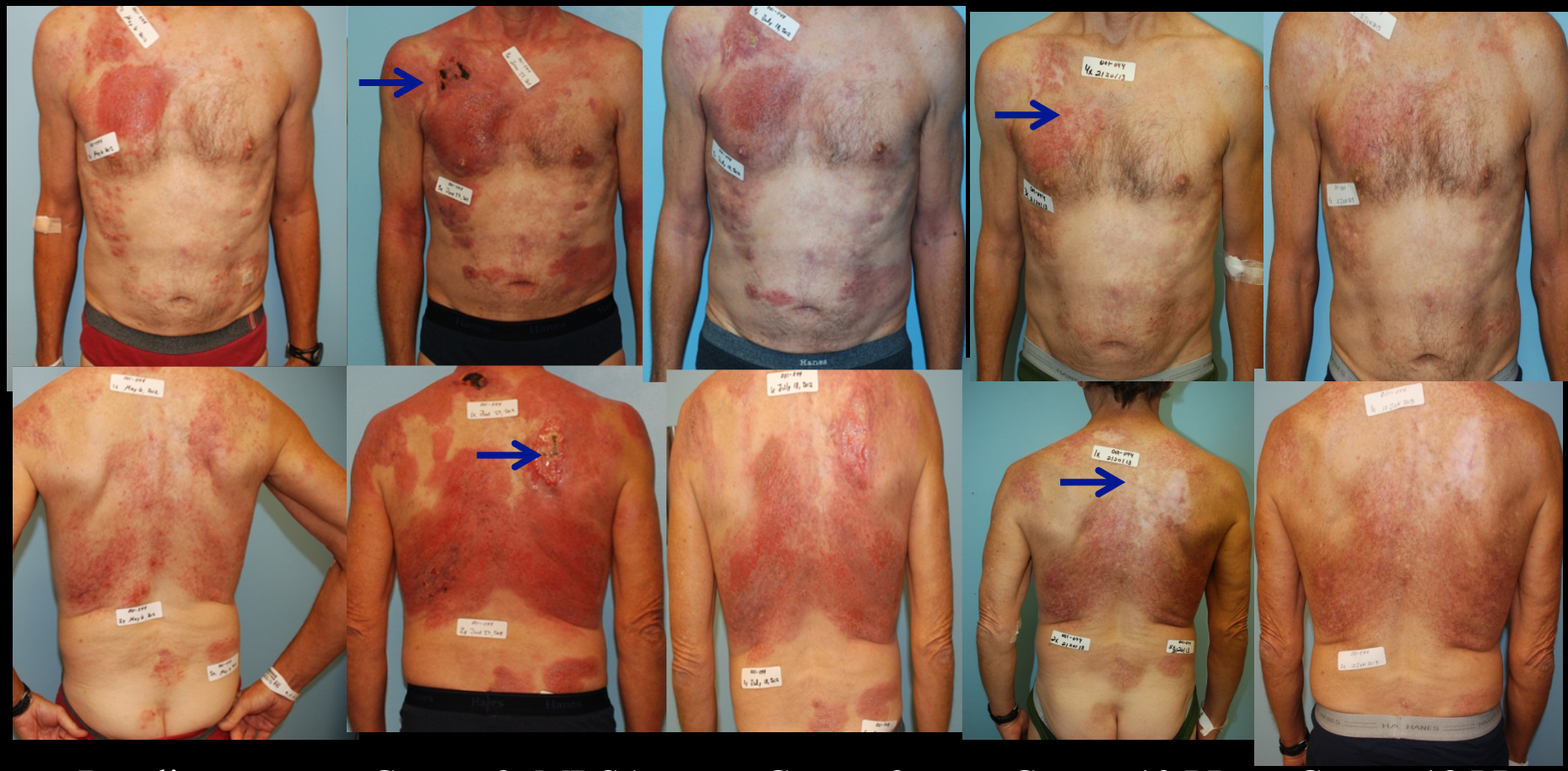
Baseline C4 C7 Term

71 y/o w SS - ECP IFN - NR

- C4: Blood PR, spongiotic dermatitis & MF,
- Dose reduced 1.2 mg/kg
- C7: Rash improved, Pruritus 0
- C7- PR skin/CR blood
- Grade 2 PN stopped BV



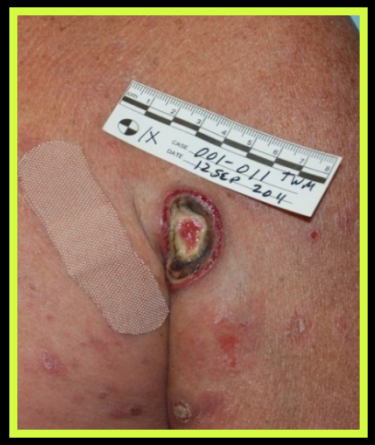
Pt 44- Folliculotropic MF T3 failed NM, Bexarotene
C2 flair - new areas, MRSA+& ulcers
C13 PR ongoing at end of treatment C18

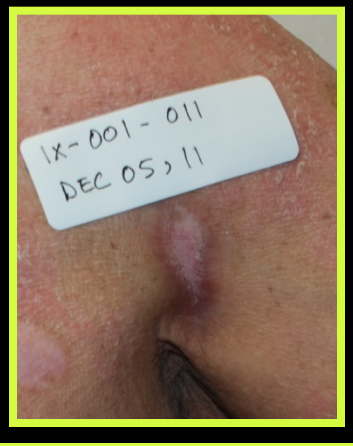


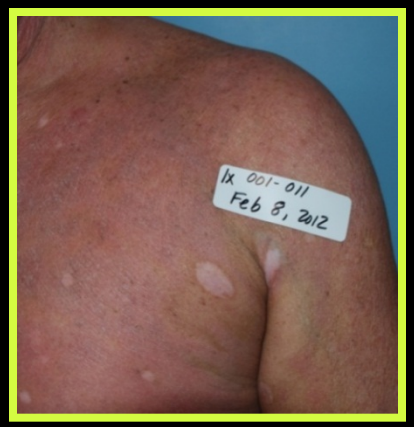
Baseline | Course 2 MRSA+ | Course 3 | Course 13 PR | Course 18 PR

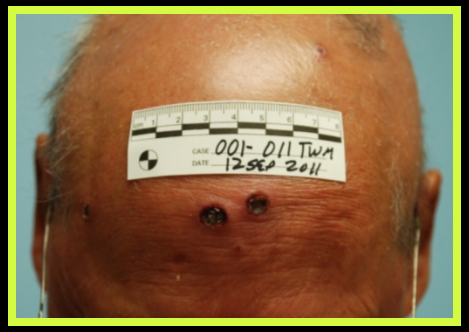
Pt 11: 550 Lyp lesions, ALCL, patch T1 MF
CD30 Expression of 30% vs 5%

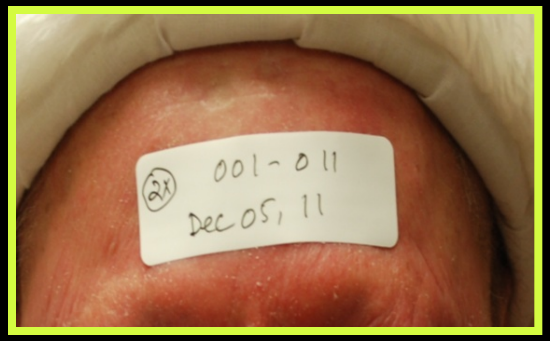
Baseline | **C5 D1** | **C8D1**

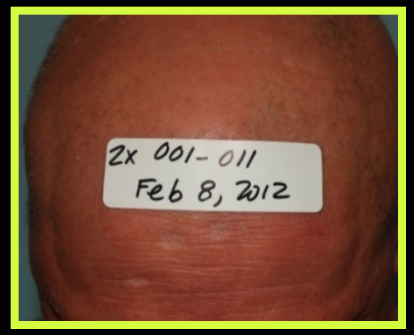


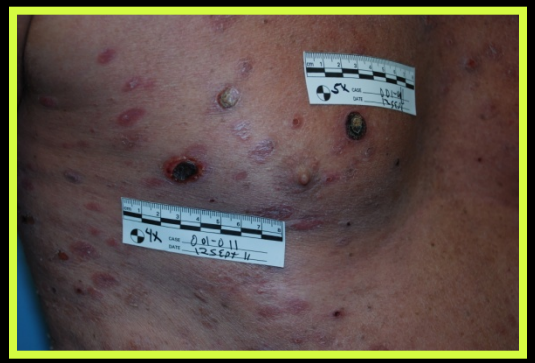


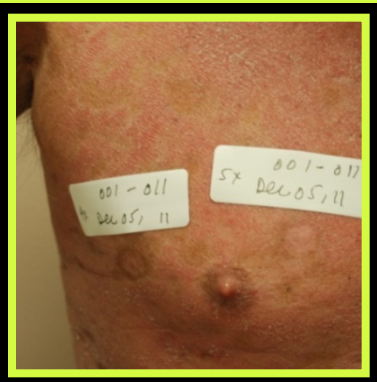


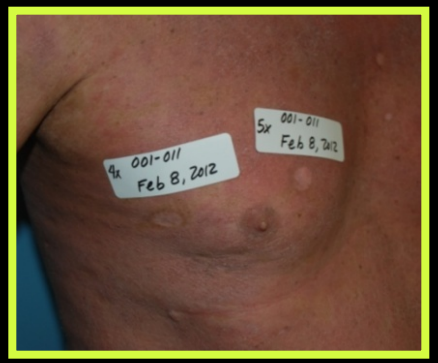




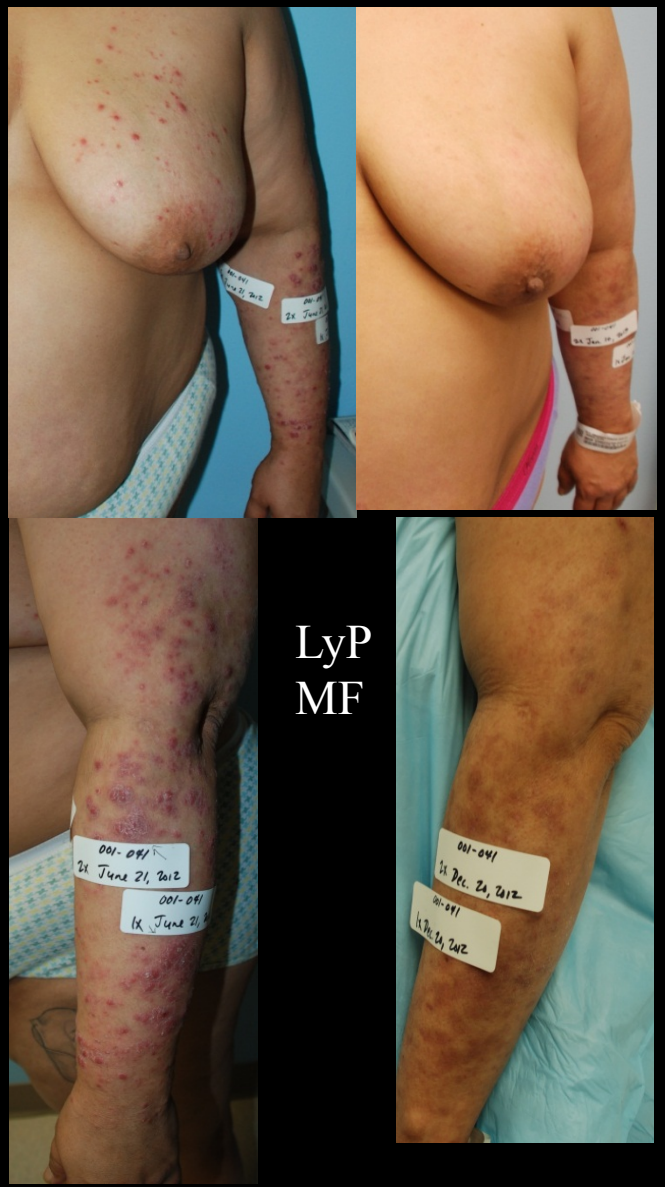








LyP and MF (T1)



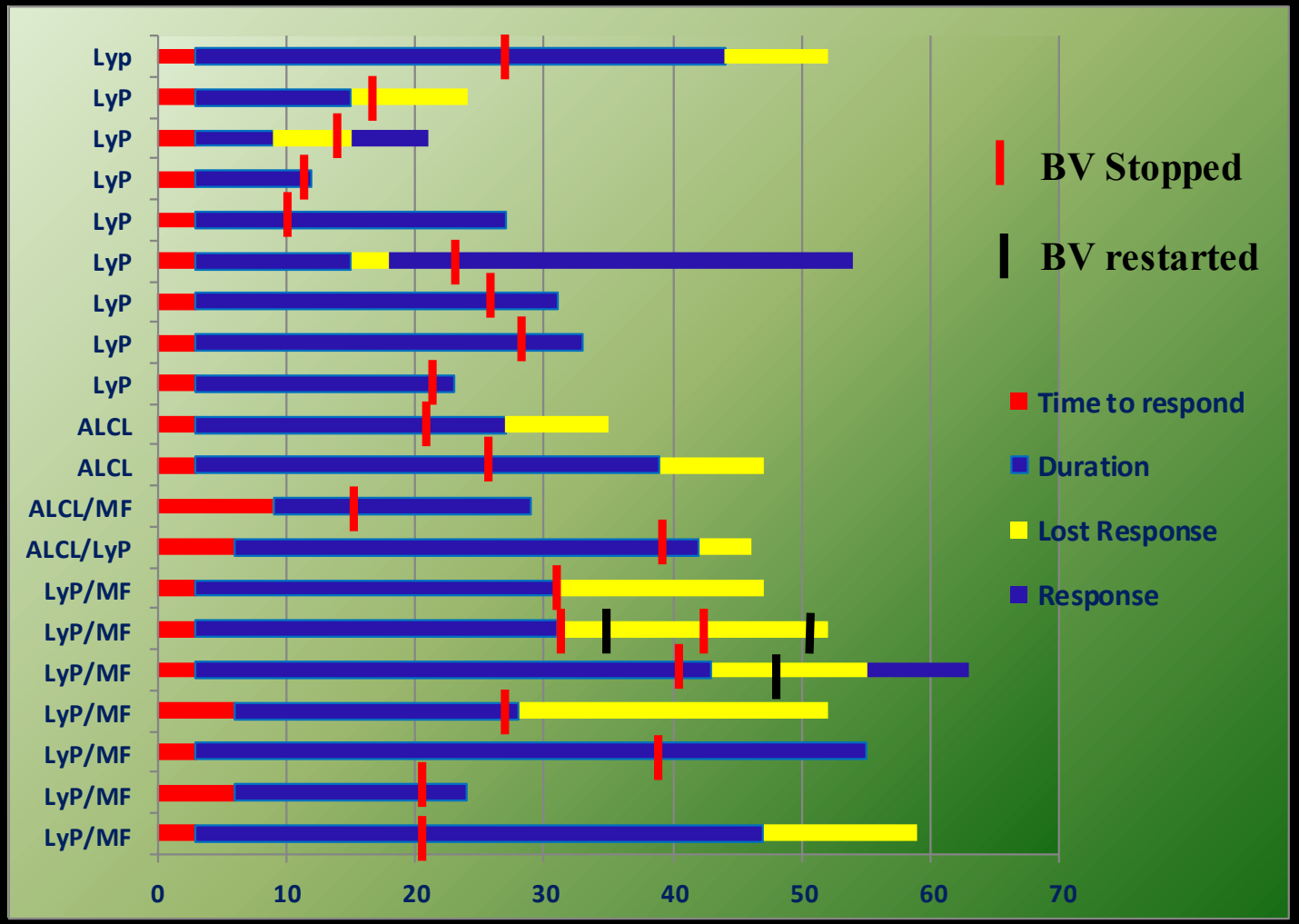
- BL 434 Lyp & MF mSWAT 5.5
- D1-2 Gr 2 infusion reactions
- D4-7 Lyp CR, MF (PR)- G1 PN
- D 8-11 Lyp 4 (PR), MF CR
- D 12 Held - G2 PN, Lyp (PR), MF CR
- D 13 Held- Lyp 332- SD, MF CR
- **PN ongoing for 64 wks**

LyP, ALCL & LyP/MF patients'
Median Time to Response - 3 wks (3-9)
Duration of Response - 26 weeks (6-44)

LyP
N= 9

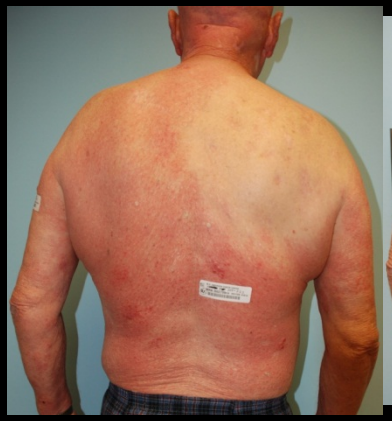
ALCL
N=2

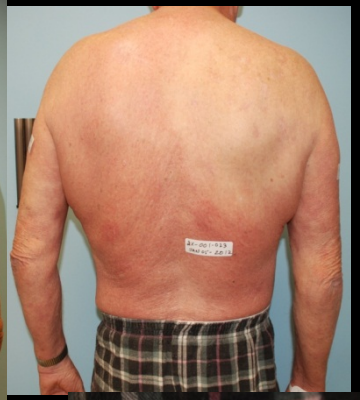
Lyp/
MF
N=7

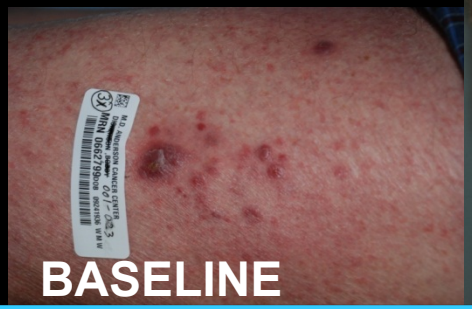


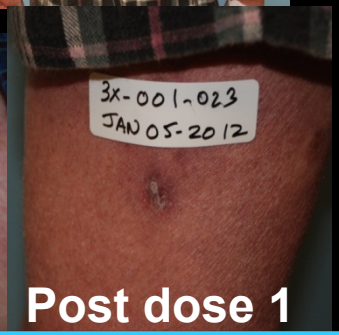
Duration in weeks

Patient 23 LyP (CR) and MF (PR)







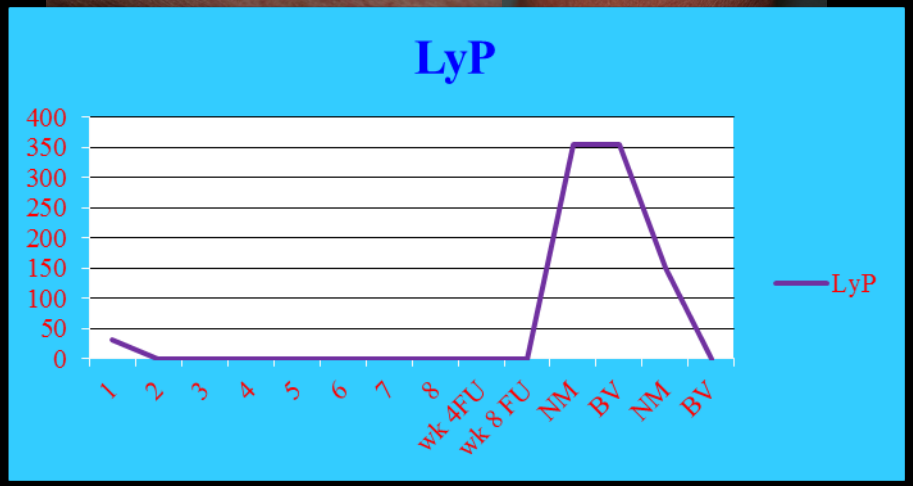


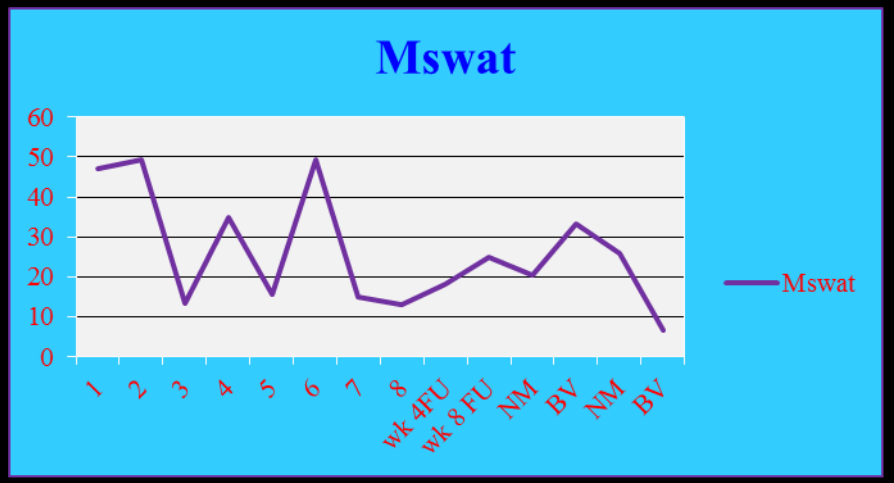
75 WM w LyP and relapsed patch MF
Radiation, methotrexate, denileukin diftitox

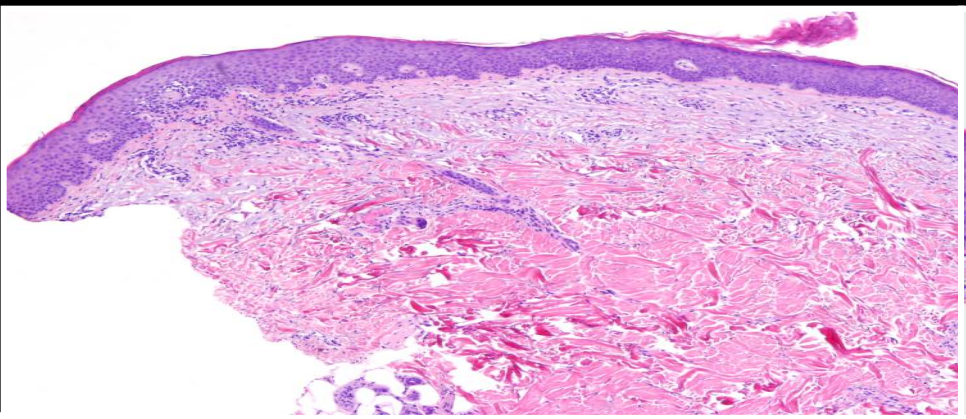
- C2 – LYP in CR, MF flared, infusion reaction
- C5 - LYP CR; 2G neuropathy- reduced 1.2 mg
- C7 - 8 - MF PR, LyP CR x 5 mos

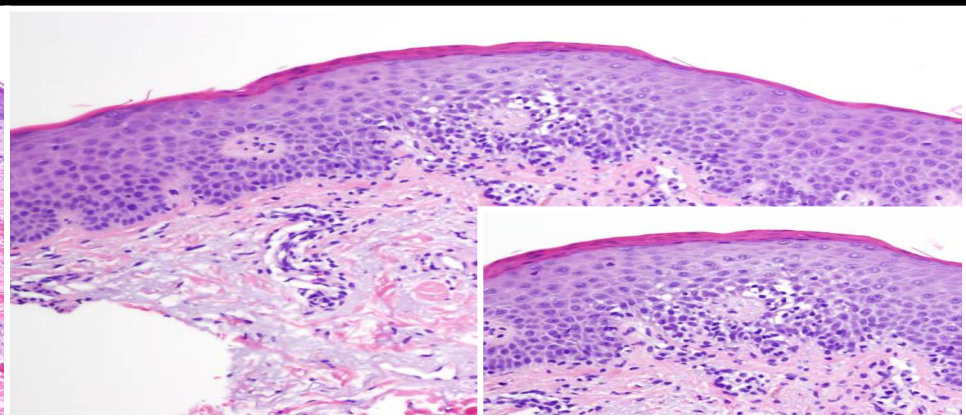
Relapsed Lyp – 355 lesions

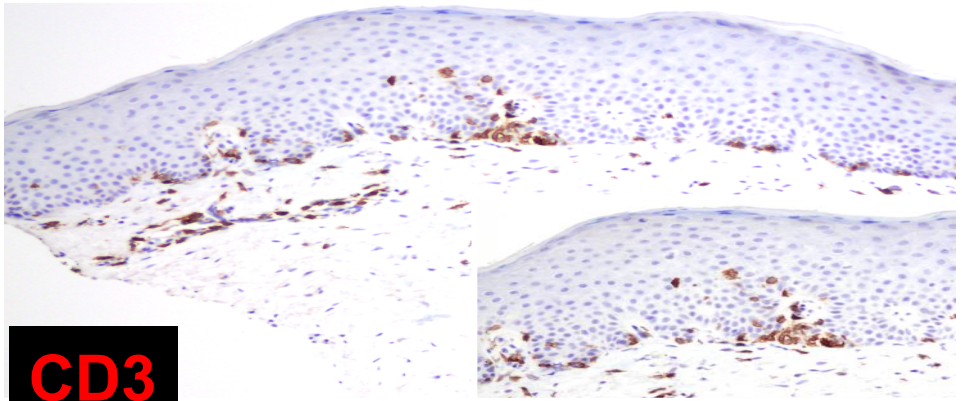
- RETREATMENT at 1.2 mg/kg + NM
- D2 – LyP CR, MF PR
- Disease control: 5 doses in 11 months
- **Variable CD30+ but same clones**

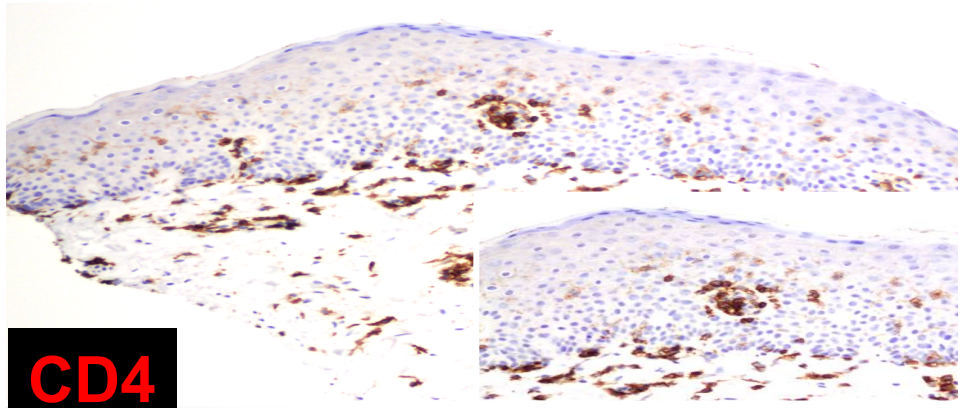


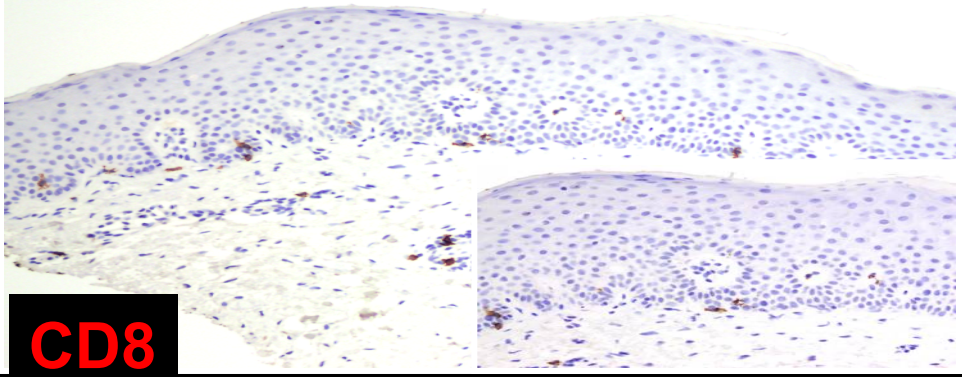


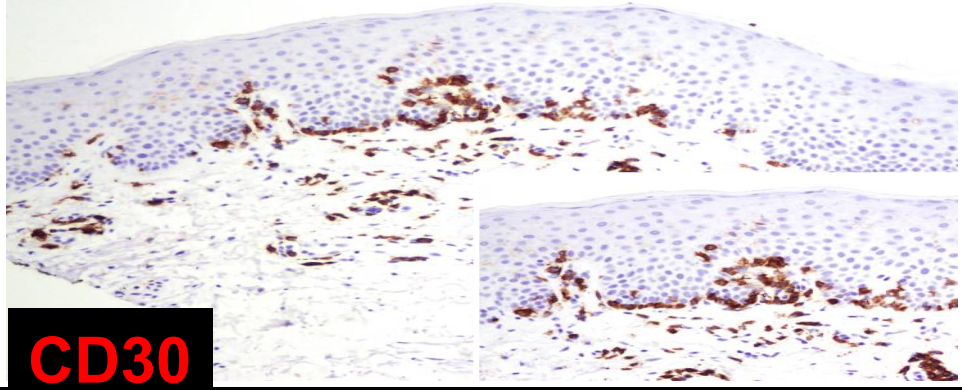




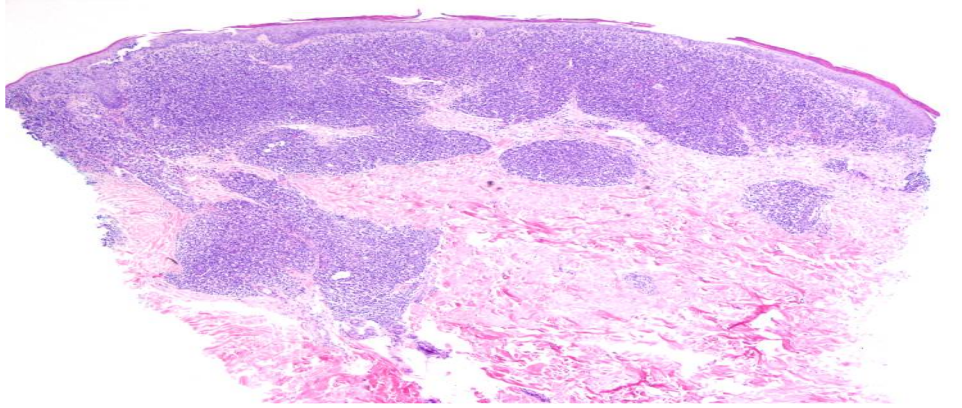


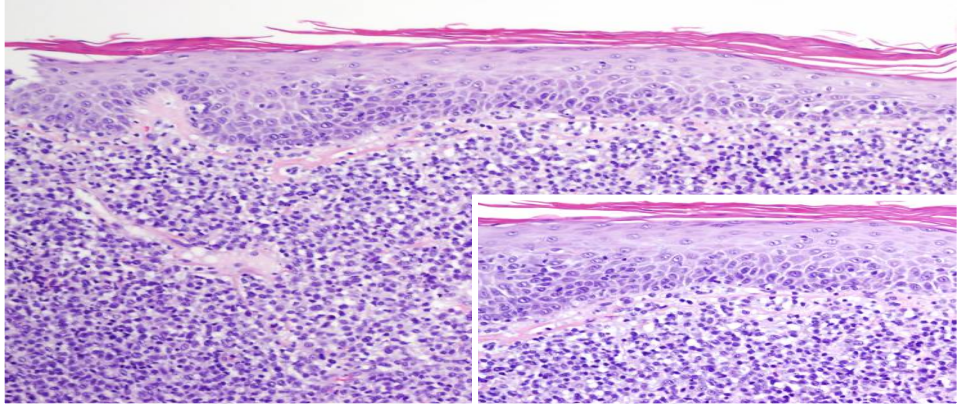


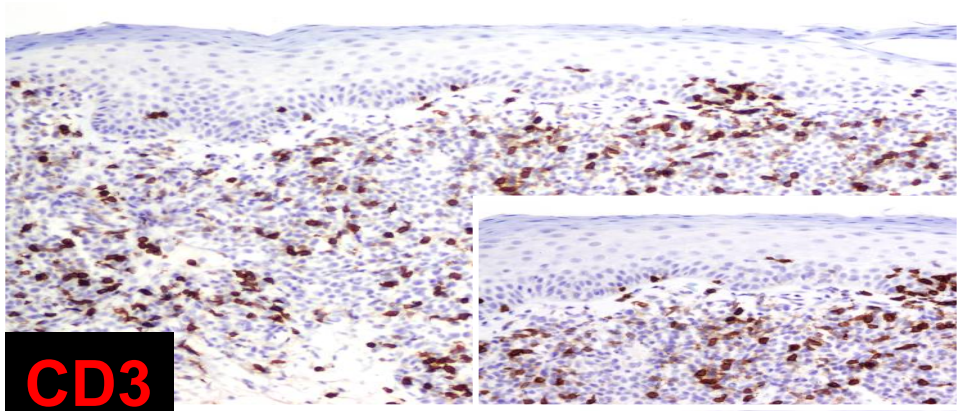


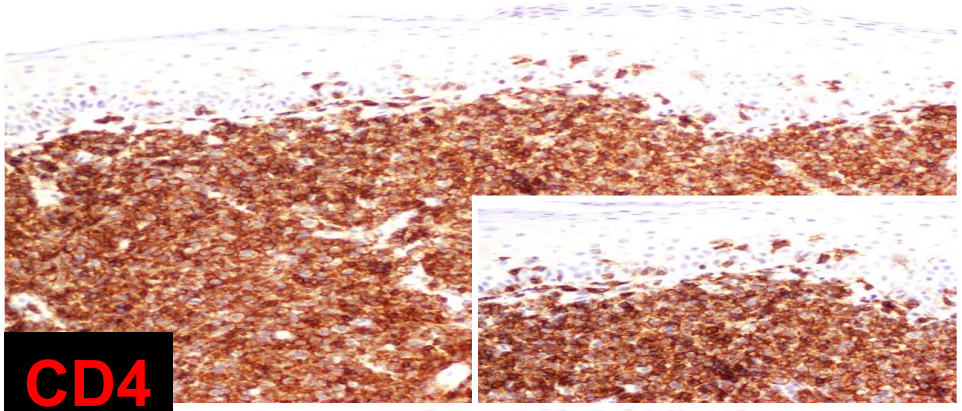


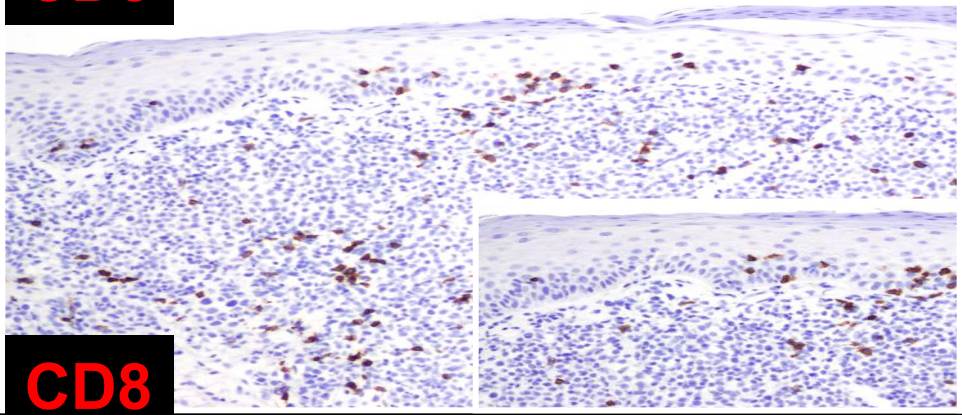
(A) Pink MF Patch right arm, punch, 12-08-2011 (662799 BD)

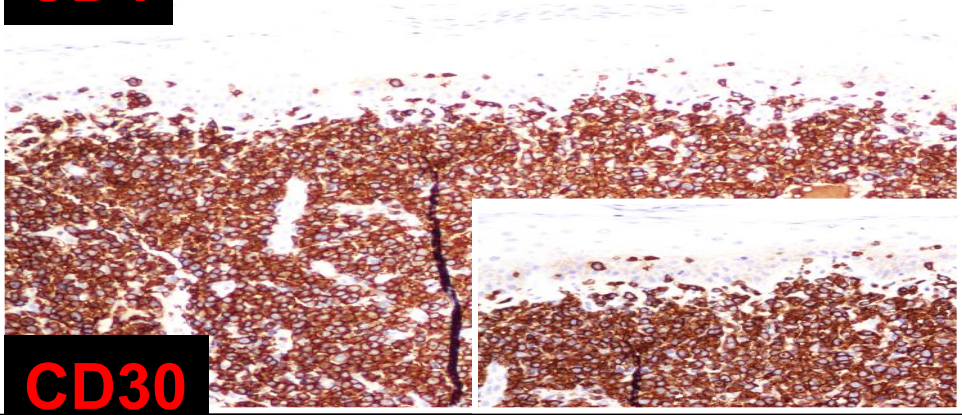








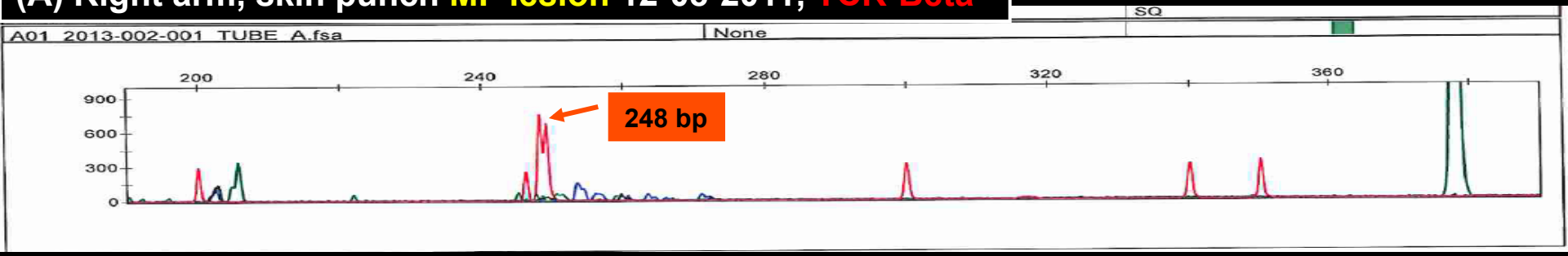




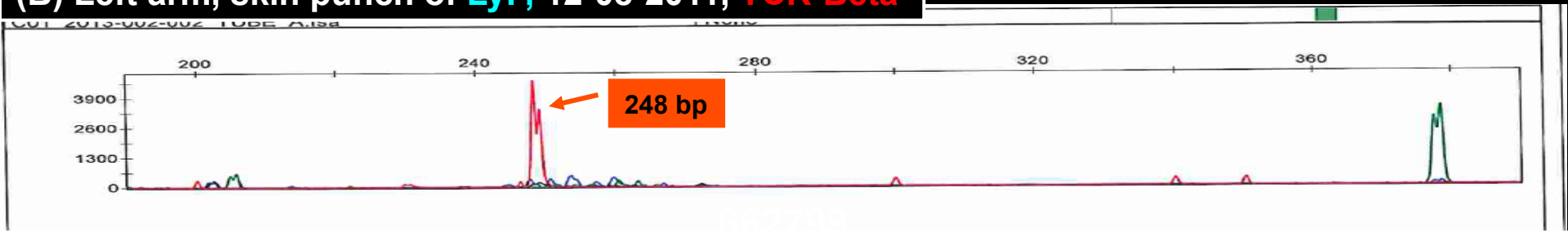
(B) LyP Papule, Left arm, punch, 12-08-2011 662799

Identical clones

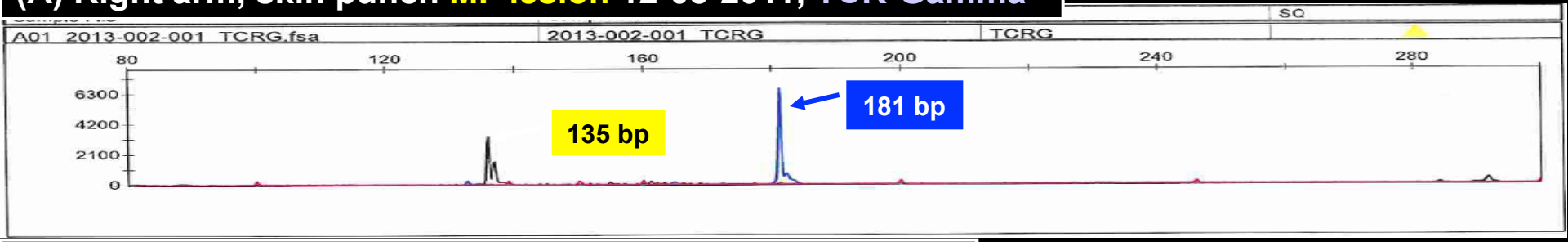
(A) Right arm, skin punch MF lesion 12-08-2011, TCR-Beta



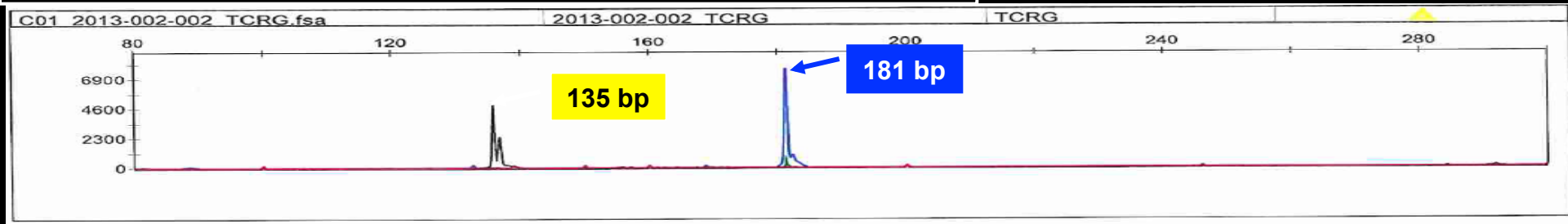
(B) Left arm, skin punch of LyP, 12-08-2011, TCR-Beta



(A) Right arm, skin punch MF lesion 12-08-2011, TCR-Gamma



(B) Left arm, skin punch of LyP, 12-08-2011, TCR-Gamma



Grade 3-5 Adverse Events

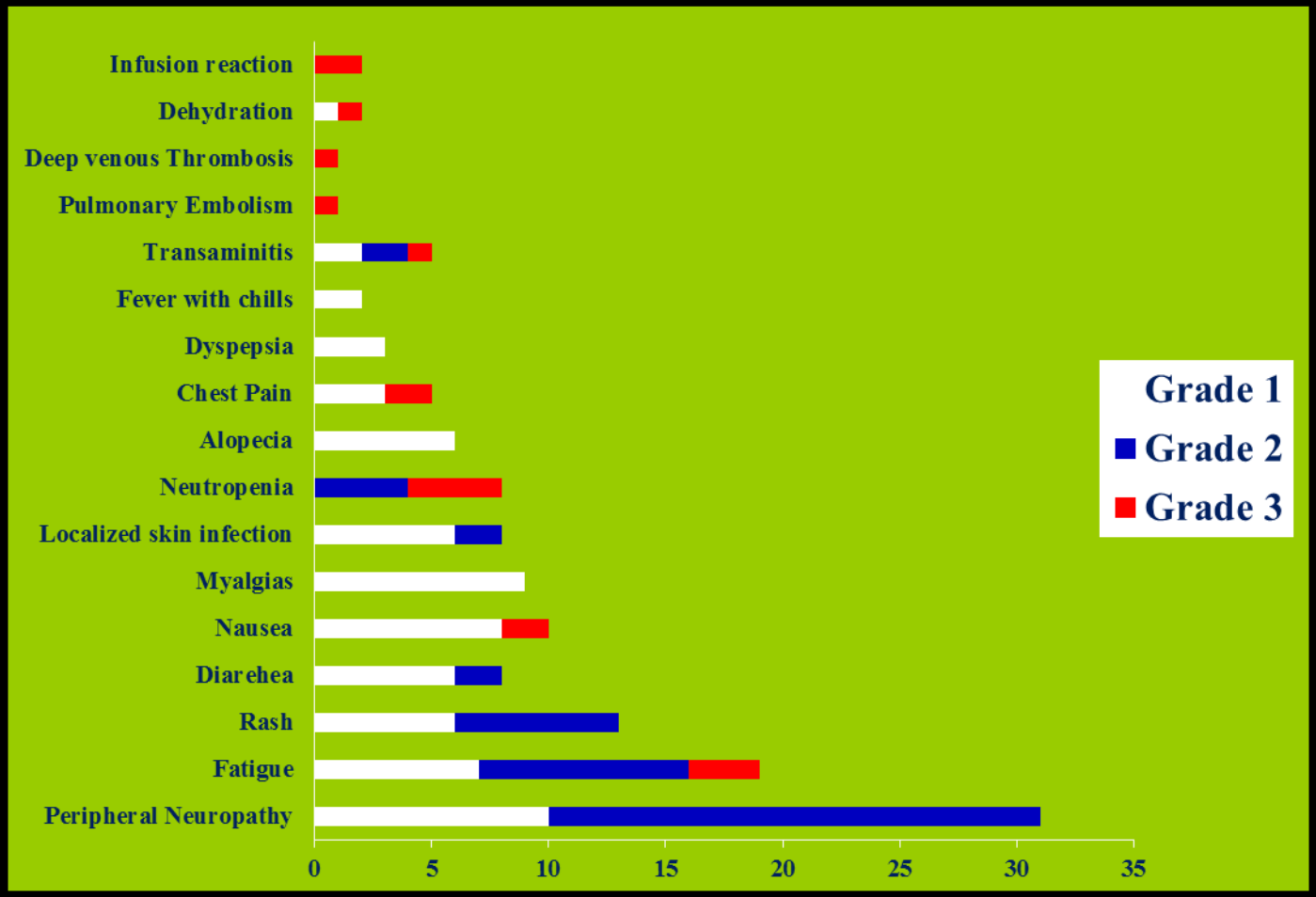
- **Grade 3 (N= 6)**

  Neutropenia (3), Nausea (2), Unstable Angina or MI (2), Infection (2), Fatigue (1), DVT (1), PE (1), LFTs (1), Dehydration (1), arthralgia (2)

Six withdrawals were for:

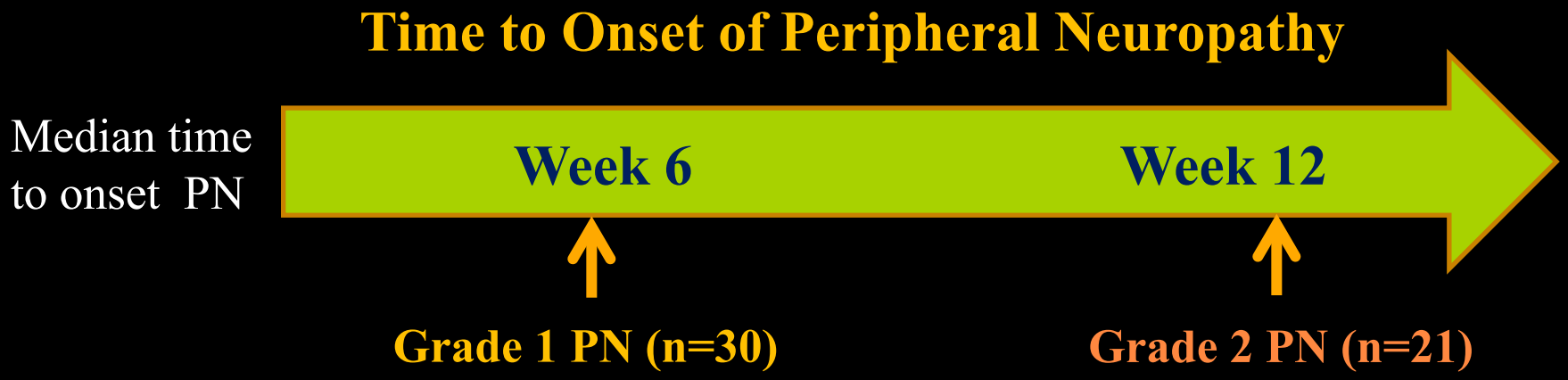
- One death sepsis in elderly ALCL tumor pt dose 1 – Gr5
- One death after urosepsis – Gr5
- One infusion reaction – withdrew consent D2
- One severe fatigue/skin pain 70% CD30 w/d consent D4
- One Unstable Angina or MI after D7
- One T-MF ineligible cord compression - entry PET CT

Number of patients (n=54) with Adverse Events by Grade



Peripheral Neuropathy (PN) Summary

- 65 % (31/48) of patients reported one event of PN
- Median Duration of PN is 60 wks (R 3-95)
- G2 PN managed with dose reductions 1.2 mg/kg (n=12)
- Resolution of PN 45% (14/31)
- Unresolved ongoing PN in 17/31 (55%)



- Median time to resolution or improvement 41.5wks

Conclusions

- Brentuximab vedotin is highly active in CD30+ CTCL
- Overall response of 73% for all patients, 100% for primary cutaneous ALCL tumors and lymphomatoid papulosis.
- ORR 54% in Mycosis fungoides, irrespective of CD30
- Flares - MF starting therapy, LyP during or after

- Median Time to Response - MF 12 wks, LyP 3 wks
- Median Duration of Response - MF 32 wks, LyP 26 wks
- Common Side effects: Neuropathy (65%), fatigue (41%), drug rash (27%)

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