

Source of data	Therapies	Patients (n)	CR/m* (%)	PR/m* (%)	Response/m* (%)	NR/m* (%)	Treatment Failure/m* (%)
All Therapies		344	125/414 (30)	89/305 (29)	33/150 (22)	180/461 (39)	163/367 (44)
SLR-1st	All Therapies	120	42/106 (40)	40/106 (38)	NA	24/106 (23)	47/109 (43)
SLR-2nd	> All Therapies	41	15/40 (38)	17/40 (43)	NA	8/40 (20)	19/39 (49)
Siltux - Phase II Toci - Open label	All Therapies (siltuximab, corticosteroids) All Therapies (tocilizumab)	79 26	1/79 (1) NA	17/79 (22) NA	NA 12/23 (52)	61/79 (77) 11/23 (48)	30/79 (38) NA
France	All Therapies	27	10/18 (56)	4/18 (22)	13/24 (54)	15/42 (36)	15/42 (36)
MDACC	All Therapies	43	16/73 (22)	29/73 (40)	NA	28/73 (38)	NA
TAFRO CRs	All Therapies	49	41/98 (42)	16/98 (16)	8/98 (8)	33/98 (34)	52/98 (53)
Corticosteroid Monotherapy		117	17/97 (18)	3/51 (6)	11/42 (26)	61/114 (54)	62/115 (54)
SLR-1st	Corticosteroid monotherapy	47	12/44 (27)	21/44 (48)	NA	11/44 (25)	21/45 (47)
SLR-2nd	Corticosteroid monotherapy	2	1/2 (50)	1/2 (50)	NA	0/2 (0)	1/2 (50)
Siltux - Phase II	Corticosteroid monotherapy (part of best supportive care)	26	0/26 (0)	0/26 (0)	NA	26/26 (100)	14/26 (54)
France	Corticosteroid monotherapy	17	NA	NA	9/17 (53)	8/17 (47)	8/17 (47)
TAFRO CRs	Corticosteroid monotherapy	25	4/25 (16)	3/25 (12)	2/25 (8)	16/25 (64)	18/25 (72)
Corticosteroid or Cytotoxic Chemotherapy, Not distinguished (MDACC)		19	2/19 (11)	10/19 (53)	NA	7/19 (37)	NA
Cytotoxic Chemotherapy, Any Time Used		135	51/124 (41)	20/58 (34)	7/35 (20)	29/131 (22)	44/105 (42)
SLR-1st	Cytotoxic chemotherapy (any time used) > Cyclophosphamide-regimen (any time used, including with rituximab)	47 23	19/43 (44) 9/22 (41)	16/43 (37) NA	NA NA	8/43 (19) NA	19/43 (44) 9/21 (43)
SLR-1st	> Rituximab (without a cytotoxic agent) > Non-cyclophosphamide based cytotoxic regimen	9 12	5/8 (63) 5/11 (45)	NA NA	NA NA	NA NA	1/8 (13) 7/12 (58)
SLR-1st	> Chemotherapy with radiation therapy	2	0/1 (0)	NA	NA	NA	1/1 (100)
SLR-1st	> Chemotherapy NOS	1	0/1 (0)	NA	NA	NA	1/1 (100)
SLR-2nd	Cytotoxic chemotherapy (any time used) Cyclophosphamide-based cytotoxic chemotherapy	23 14	9/23 (39) 9/14 (64)	8/23 (35) 2/14 (14)	NA 2/14 (14)	6/23 (26) 1/14 (7)	12/22 (55) 4/14 (29)

TAFRO CRs	Rituximab with a cytotoxic agent	1	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)
MDACC	Rituximab with or without a cytotoxic agent	25	5/25 (20)	12/25 (48)	NA	8/25 (32)	NA
TAFRO CRs	Rituximab without a cytotoxic agent	10	7/10 (70)	1/10 (10)	1/10 (10)	1/10 (10)	4/10 (40)
France	Rituximab without a cytotoxic agent	7	NA	NA	4/7 (57)	3/7 (43)	3/7 (43)
France	Non-cyclophosphamide, non-rituximab based cytotoxic regimen (etoposide)	5	0/5 (0)	4/5 (80)	NA	1/5 (20)	1/5 (20)
TAFRO CRs	Non-cyclophosphamide, non-rituximab based cytotoxic regimen	3	1/3 (33)	1/3 (33)	0/3 (0)	1/3 (33)	1/3 (33)

Anti-IL-6 mAb Without Cytotoxic Agent		147	43/121 (36)	29/95 (31)	12/23 (52)	56/144 (39)	32/100 (32)
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SLR-1st	Anti-IL-6 mAb (only when without cytotoxic agent)	11	10/11 (91)	1/11 (9)	NA	0/11 (0)	2/11 (18)
SLR-1st	> Tocilizumab with or without corticosteroids	9	8/9 (89)	NA	NA	NA	1/9 (11)
SLR-1st	> Siltuximab with or without corticosteroids	2	2/2 (100)	NA	NA	NA	1/2 (50)
SLR-2nd	Anti-IL-6 mAb (only when without cytotoxic agent)	5	2/5 (40)	NA	NA	NA	2/5 (40)
Toci - Open label	Tocilizumab with or without corticosteroids	26	NA	NA	12/23 (52)	11/23 (48)	NA
France	Tocilizumab with or without corticosteroids	10	10/10 (100)	0/10 (0)	NA	0/10 (0)	1/10 (10)
TAFRO CRs	Tocilizumab with or without corticosteroids	20	10/20 (50)	5/20 (25)	0/20 (0)	5/20 (25)	10/20 (50)
Siltux - Phase II	Siltuximab with or without corticosteroids	53	1/53 (2)	17/53 (32)	NA	35/53 (66)	16/53 (30)
MDACC	Siltuximab with or without corticosteroids	21	9/21 (43)	7/21 (33)	NA	5/21 (24)	NA
TAFRO CRs	Siltuximab with or without corticosteroids	1	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	1/1 (100)

Immunomodulators Without Cytotoxic Agent		27	9/26 (35)	1/17 (6)	3/17 (18)	8/26 (31)	10/26 (38)
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SLR-1st	Immunomodulators (only when without cytotoxic agent)	5	0/4 (0)	2/4 (50)	NA	2/4 (50)	3/4 (75)
SLR-2nd	Immunomodulators (only when without cytotoxic agent)	5	2/5 (40)	3/5 (60)	NA	0/5 (0)	0/5 (0)
TAFRO CRs	Immunomodulators - Cyclosporine A (only when without cytotoxic agent)	8	3/8 (38)	0/8 (0)	3/8 (38)	2/8 (25)	2/8 (25)
TAFRO CRs	Immunomodulators - Others (only when without cytotoxic agent)	9	4/9 (44)	1/9 (11)	0/9 (0)	4/9 (44)	5/9 (56)

Other		16	3/13 (23)	3/7 (43)	NA	5/13 (38)	12/15 (80)
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SLR-1st	Others	3	1/1 (100)	0/1 (0)	NA	0/1 (0)	1/3 (33)
SLR-2nd	Others	6	1/5 (20)	2/5 (40)	NA	2/5 (40)	4/5 (80)

TAFRO CRs	Others	7	1/7 (14)	3/7 (43)	0/7 (0)	3/7 (43)	7/7 (100)
No Treatment/Follow Up Only		18	0/14 (0)	0/11 (0)	NA	14/14 (100)	11/14 (79)
SLR-1st	No treatment/follow up only	7	0/3 (0)	0/3 (0)	NA	3/3 (100)	1/3 (33)
France	No treatment/follow up only	3	0/3 (0)	0/3 (0)	NA	3/3 (100)	2/3 (67)
MDACC	No treatment/follow up only	8	0/8 (0)	0/8 (0)	NA	8/8 (100)	8/8 (100)
Total number of regimens evaluated (m)		479					

Supplementary Appendix 1. iMCD Clinical Case Series. Literature review of published case reports, small series, and clinical trials were compiled to inform and substantiate the experience and opinion of the CDCN Working Group authors. Cytotoxic chemotherapy regimens described may include the use of rituximab. n = number of subjects treated in each treatment regimen category; m = total number of regimens evaluated (479); m* = number regimens assessed for stated outcome. CR, complete response; PR, partial response; Response, response with depth undefined; NR, no response. Source Data: SLR-1st, systematic literature review - first line therapy¹; SLR-2nd, systematic literature review - second line therapy¹; Siltux Phase II, siltuximab Phase II clinical trial²; Toci - Open Label, tocilizumab open label reports³; France, report by French group⁴; MDACC, report by MD Anderson Cancer Center⁵; TAFRO CRs, TAFRO case reports.⁶⁻⁴⁸

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Therapy	Patients (n)	Response (%)	No Response (%)	Treatment Failure (%)
All Therapies	49	65/98 (66)	33/98 (34)	52/98 (53)
Corticosteroid Monotherapy	25	9/25 (36)	16/25 (64)	18/25 (72)
Cyclophosphamide-based cytotoxic chemotherapy	14	13/14 (93)	1/14 (7)	4/14 (29)
Rituximab with Cytotoxic Agent	1	1/1 (100)	0/1 (0)	0/1 (0)
Rituximab without Cytotoxic Agent	10	9/10 (90)	1/10 (10)	4/10 (40)
Cytotoxic Regimen (without Cyclophosphamide or Rituximab)	3	2/3 (67)	1/3 (33)	1/3 (33)
Tocilizumab with or without Steroids	20	15/20 (75)	5/20 (25)	10/20 (50)
Siltuximab with or without Steroids	1	1/1 (100)	0/1 (0)	1/1 (100)
Cyclosporine A (without Cytotoxic Agent)	8	6/8 (75)	2/8 (25)	2/8 (25)
Immunomodulators – Other than Cyclosporine A (without Cytotoxic Agent)	9	5/9 (56)	4/9 (44)	5/9 (56)
Other	7	4/7 (57)	3/7 (43)	7/7 (100)

Supplementary Appendix 2. iMCD-TAFRO Cases. These were compiled from published case reports and small series. n = number of subjects treated in each treatment regimen category, with a total of 98 regimens evaluated. Other includes: plasma exchange (n=3), plasma exchange + corticosteroids (n=2), Polymyxin B-immobilized fiber column direct hemoperfusion and cytokine absorption (n=1), allogeneic stem cell transplant (n=1). Please refer to **Supplementary Appendix 1** for complete list of references.