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SUPPLEMENTARY MATERIAL

Small molecules in idiopathic inflammatory myopathies: a systematic review and a multicenter case series about Janus kinase inhibitors and apremilast

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Supplementary Table 1. Supplemental demographic and clinical data of patients treated with targeted synthetic disease modifying anti-rheumatic drugs from the literature.

Drug	Author, study, year	Patients (number, diagnosis, age, gender, *AB*)	Previous IS	Concomitant IS	Skin	Muscle	Joints	Lungs	GI tract	Side effects
BAR	**Delvino**, case report, 2020 [37]	1 DM 58 f	AZA, IVIg, MTX, PDN	PDN	✓	✓	✓			none
	Chen, case report, 2022 [38]	1 DM 25 f *MDA5*	MMF, TAC	PDN, TAC	✓					none
	Fischer, case report, 2022 [39]	3 DM *1 MDA5* *1 NXP2*	ADA, AZA, IVIg, MTX, PDN,	IVIg, PDN	✓	✓				Orolabial HSV
	Landon-Cardinal, pilot study, 2022 [40]	12 DM Mean age 53 f = 11 *3 MDA5* *2 NXP2* *1 SAE* *2 TIF1γ*	AZA, CSP, CYC, IVIg, MMF, MTX, PDN, PEX, RTX, TAC, none	IVIg, MMF, PDN, ns	✓	✗				Thromboembolic event, febrile neutropenia
RUX	**Hornung**, case report, 2014 [42]	1 DM	AZA, IVIg, MMF, PDN	IVIg, MMF, PDN	✓	✓				none

		72 f								
	Ladislau, case report, 2018 [43]	4 DM Mean age 66.7, f *1 SAE* *3 TIF1γ*	AZA, CYC, IVIg, MMF, MTX, PDN, PEX, RTX	IVIg, PDN	✓	✓				none
	Fetter, case report, 2020 [45]	1 DM 40 f *TIF1γ*	AZA, CSP, CYC, ETN, IVIg, MMF, MPDN ev, MTX, PDN, RTX	PDN	✓ alopecia					none
	Jalles, case report, 2020 [44]	1 DM 60 f *MDA5*	CYC, IVIg, MPDN ev, PDN	PDN	✓	✓		✓		Malignancy
	Landon-Cardinal, pilot study, 2022 [40]	4 DM Mean age 62.5, f *1 SAE* *3 TIF1γ*	AZA, IVIg, MMF, MTX, PDN, PEX	IVIg, MMF, PDN	✓	✗				Thromboembolic event, febrile neutropenia
TOF	**Paik**, case report, 2016 [10]	1 DM 55 f	AZA, IVIg, MMF, MTX, PDN, RTX	PDN	✓	✓	✓			none
	Hornig, case report, 2018 [11]	1 CADM	CSP, CYC, IVIg, MMF,	PDN	✓			✓		Zoster reactivation

		32 m *MDA5*	PDN, PEX, RTX							
	Kurasawa, case report, 2018 [58]	5 DM Mean age 60.6 f = 3 *MDA5*	/	CSP, CYC, MPDN ev, PDN				✓		CMV reactivation, Zoster reactivation, adenovirus cystitis, bacterial and fungal infections, lymphoproliferative disease with EBV activation, pancytopenia
	Kurtzaman, case series, 2018 [12]	2 DM / 1 CADM Mean age 40, f	AZA, IVIg/SCIg, MTX, MMF, PDN, RTX	HCQ, none	✓ puritus	✓				none
	Chen, open label study, 2019 [59]	18 ADM Mean age 47.6 *MDA5*	CSP, CYC, PDN, TAC	PDN				✓		Liver function abnormality, urinary tract infection, possible invasive fungal infection
	Siamak, case series, 2019 [8]	3 DM / 1 CADM Mean age 54.6, 2 f / 59 m *1 SAE, 2 TIF1γ / 1 TIF1γ*	AZA, IVIg, MMF, MTX, PDN, TAC	IVIg, PDN	✓	✓	✓			none

	Wendel, case report, 2019 [13]	2 DM Mean age 54.5, f *1 MDA5* *1 Mi2*	AZA, CSP, IVIg, MTX, PDN, RTX, TAC	PDN	✓		✓	✓		none
	Kato, case report, 2019 [60]	1 DM 44 f *MDA5*	CYC ev, MPDN ev, PDN, PEX, TAC	CSP, PDN				✓		none
	Babaoglu, case report, 2019 [31]	1 PM 54 f	AZA, CSP, IVIg, MPDN ev, MTX, PDN, RTX, TAC	IVIg, MPDN ev, PDN		✓				none
	Conca, case report, 2020 [29]	1 ASS 54 f *Jo1*	AZA, IVIg, MPDN ev, PDN, TAC	MPDN ev, PDN				✓		CMV reactivation
	Pineton De Chambrun, case report, 2020 [28]	1 ASS 55 m *PL12*	MPDN ev	ECMO, PDN, TAC				✓		none
	Ishikawa, case report, 2020 [14]	1 CADM 57 f *MDA5*	AZA, CYC, PDN, TAC	PDN	✓		✓	✓		none

	Ohmura, case report, 2020 [15]	1 DM 55 m *MDA5*	CYC, IVIg, MPDN ev, MTX, PDN, TAC	CYC, PDN, TAC	✓			✓		CMV reactivation, skin infection, lymphopenia
	Navarro, clinical letter, 2020 [16]	2 DM Mean age 49.5, f *1 NXP2* *1 TIF1γ*	CSP, IVIg, MPDN ev, IVIg, MTX, PDN, RTX, TAC	none	✓	✓				Zoster reactivation
	Takatani, case report, 2020 [61]	1 DM 56 f *MDA5*	CSP, CYC, MPDN ev PDN, PEX, TAC	CYC, PDN				✓		none
	Crespo Cruz, case report, 2020 [17]	1 ADM 49 f	AZA, IVIg, MMF, MTX, PDN, RTX, TAC	PDN	✓					none
	Hosokawa, case report, 2021 [18]	1 DM 66 f *MDA5*	CYC ev, PDN, PEX, TAC	PDN	✓			✓		none
	Shneyderman, case series, 2021 [19]	3 DM Mean age 46.6, f *2 NXP2*	/	/	✓	✓				none

		1 TIF1γ								
	Paik, prospective open-label study, 2021 and long-term extension, 2022 [20, 21]	10 DM Mean age f = 7 *1 Mi2* *2 NXP2* *7 TIF1γ*	AZA, IVIg, MMF, MTX, PDN, TAC, RTX	none	✓ All patients met ACR/EULAR myositis response criteria (50% moderate improvement, 50% minimal improvement)					Recurrent urinary tract infections
	Tseng, case report, 2022 [30]	1 ASS 69 m *EJ*	none	PDN, RTX				✓ ARDS		none
	Luo, case report, 2022 [23]	1 DM 56 f *MDA5*	CSP, CYC, PDN	PDN	✓			✓		Gangrenous cholecystitis
	Min, retrospective study, 2022 [26]	5 ADM, 4 DM (3 JDM) Mean age 41.1 f = 11	AZA, CSP, IFX, IVIg, MMF, MTX, PDN, RTX, SCIg	IVIg, MTX, PDN	✓	✓				Orolabial HSV
	Castillo, case report, 2022 [24]	1 DM 30 f *Mi-1 and TIF1γ*	AZA, IVIg, MTX	IVIg	✓		✓			none

	Takanashi, case report - review, 2022 [32]	1 CADM 48 m *MDA5*	CSP, CYC ev, IVIg, MMF, MPDN ev, PDN, PEX, TAC	/				✗		Bacterial pneumonia, fungal infection, sepsis
	Fan, retrospective analysis, 2022 [36]	26 DM Mean age 55.4 f = 15 *MDA5*	PDN, ns	IVIg, PDN, PEX, ns	✓ 6-month and 1-year all-cause mortality rates were significantly lower (in ILD and RP-ILD) compared to those of patients treated with TAC					Pulmonary fungal infections, oral candida infection, EBV and CMV reactivation, Zoster infections, sepsis due to pulmonary infection, intermuscular vein thrombosis
	Plante, retrospective review, 2022 [25]	3 DM (1 JDM) Mean age 40.2 f = 3 *1 Jo1* *1 SAE*	AZA, CSP, IVIg, MMF, MTX, PDN, RTX, TAC, topical steroids	IVIg, MTX, PDN, TAC, topical steroids	✓	✓	✓	✗	✓	none
	Hiraoka, case report, 2022 [35]	1 CADM 71 m *MDA5*	/	CYC, MPDN ev, PDN, TAC				✗		CMV reactivation
	Robert, case report, 2023 [22]	1 DM 56 f	CYC, GC, IVIG, MTX	GC, IVIG	✓					none

		NXP2								
	Wang, open-label trial, 2023 [27]	14 DM Mean age 47.3 f = 9 *MDA5*	none	GC, MPDN ev	✓ 2 major improvement ✓ 7 moderate improvement ✓ 1 minimal improvement ✗ 4 deaths (respiratory failure)					Zoster reactivation, respiratory infection
	Shirai, retrospective study, 2023 [33]	13 out of 33 DM Mean age 53.8 *MDA5*	IVIg, MPDN ev, PEX, RTX	MPDN ev, PEX, RTX	✓ significant improvement in survival ✗ 2 deaths (exacerbation of ILD)					CMV reactivation, haemorrhagic cystitis, BK and adenovirus viremia, *Aspergillus* pneumonia, *Nocardia* infection, cytopenia
	Ida, case series, 2023 [34]	6 DM Mean age 55.5 f = 3 *MDA5*	/	CYC, MPDN ev, PEX, TAC	✓ 4 patients improved after dose escalation of TOF ✗ 2 deaths (ILD exacerbation)					CMV reactivation, *Aspergillus* pneumonia, Zoster reactivation, HSV keratitis
APR	**Bitar,** case report, 2019 [54]	3 DM Mean age 61 f = 3	AZA, IFX, IVIg, MMF, MTX, PDN, RTX, TAC	MMF, PDN	✓	✓				Mild nausea, diarrhoea
	Charlton, case report, 2021 [55]	1 DM 50 f *TIF1γ*	AZA, IVIg, MMF, MTX, PDN, TAC	PDN	✓					none

	Konishi, phase Ib pilot study, 2022 [56]	5 DM Mean age 64 f = 4 *1 Mi2* *2 SAE* *2 TIF1γ*	CSP, PDN, TAC	/	✓					Diarrhoea, nausea, vomiting
	Bitar, non randomized-control trial, 2022 [57]	8 DM Mean age 54, f	/	/	✓					none

AB antibodies, ABA abatacept, ADA adalimumab, ADM amyopathic dermatomyositis, ANA anakinra, ARDS acute respiratory distress syndrome, ASS anti-synthetase syndrome, AZA azathioprine, BAR baricitinib, CADM clinically amyopathic dermatomyositis, CMV cytomegalovirus, CSP cyclosporine, CYC cyclophosphamide, DM dermatomyositis, DMARDs disease modifying antirheumatic drugs, EBV Epstein-Barr virus, ECMO extracorporeal membrane oxygenation, ev endovenous, f female, GC glucocorticoids, GI gastrointestinal tract, HSV herpes simplex virus, ILD interstitial lung disease (RP rapidly progressive), IS immunosuppressants, IVIg intravenous immunoglobulins, JDM juvenile dermatomyositis, m male, MAS macrophage activation syndrome, MMF mycophenolate mofetil, MPDN methylprednisolone, MTX methotrexate, ns not specified, PDN prednisone/prednisolone, PEX plasma exchange, PM polymyositis, SCIg subcutaneous immunoglobulins, RTX rituximab, RUX ruxolitinib, TAC tacrolimus, TOF tofacitinib, / not available or not reported.

The outcome of organ involvement is reported as improved (✓) or not improved/worsened (✗): the effect on specific symptoms (e.g. pruritus) or signs has been specified. An empty box indicates that patients did not suffer from that specific organ involvement, while merged boxes indicates that the authors of the article reported a common outcome for more manifestations.