Defining appropriate targets and optimal timing for a Treat-toTarget Strategy in Juvenile Dermatomyositis

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INTRODUCTION

- The management of juvenile dermatomyositis (JDM) is not standardized and no widely embraced therapeutic protocols are available.
- Furthermore, the optimal therapeutic targets as well as the ideal timing of their achievement are not established.
- Defining these aspects of the therapeutic approach would be fundamental to implement the treat-to-target (T2T) strategy.
- Objective of the study was to investigate the longitudinal trends of indicators of treatment effectiveness in a cohort of JDM patients, with the aim of identifying suitable targets and optimal timing of their achievement.

METHODS

- We reviewed retrospectively the charts of 44 patients diagnosed with JDM between 2009 and 2022, seen at our center within 6 months after disease diagnosis and followed for ≥ 6 months.
- The disease course was assessed at the following time points: baseline (diagnosis) and after 1.5, 3, 6, 12, 18 and 24 months.
- Collected data included demographic features, muscle enzymes, and the main physician- and parent-centered JDM outcome measures.
- Time to skin remission, muscle remission, normalization of muscle enzymes, inactive disease (ID) by PRINTO modified criteria, steroid discontinuation, reduction of prednisone (PDN) dose < 0.3/0.1 mg/kg/day, complete clinical response (CCR), remission, ID and low disease activity (LDA) by JDMAI1 and JDMAI2 were calculated.
- Treatment response by IMACS and PRINTO criteria, as well as longitudinal changes in JDMAI1 and JDMAI2 were also evaluated.

RESULTS

	Range	N	Value
Demographic features			
Age at diagnosis (years), mean (SD)	-	44	7.45 (4.27)
Female sex, n (%)	-	44	25 (56.82)
Initial therapy IGG, n (%)	-	44	33 (75.00)
Time to treatment start from symptoms onset (months), median (IQR)	-	44	4.22 (2.04-8.37)
Disease duration from symptoms onset (months), median (IQR)	-	44	4.36 (2.38-8.89)
Disease duration from diagnosis (months), median (IQR)	-	44	0.00 (0.00-0.33)
Clinical characteristics			
Physician Global Assessment of overall disease activity VAS, mean (SD)	0-10	39	5.17 (2.35)
Parent Global Assessment of overall wellbeing VAS, mean (SD)	0-10	42	5.14 (2.48)
MMT8, median (IQR)	0-80	43	67 (50-75)
CMAS, mean (SD)	0-52	22	36.36 (10.84)
hMC, mean (SD)	0-100	30	76.50 (16.56)
Muscle DAS, mean (SD)	0-11	44	4.86 (3.11)
Skin VAS, mean (SD)	0-10	44	3.58 (2.16)
Skin DAS, mean (SD)	0-9	44	5.23 (2.01)
Total DAS, mean (SD)	0-20	44	10.11 (4.07)
JDMAI1, mean (SD)	0-40	25	15.92 (6.74)
JDMAI2, mean (SD)	0-39	25	17.36 (6.34)
CHAQ, median (IQR)	0-3	28	0 (0-2)
Laboratory results			
MSA positivity, n (%)	-	38	23 (60.53)
ANA positivity, n (%)	-	41	22 (53.66)
CK, median (IQR)	0-150	44	180 (67-788.5)
ALT, median (IQR)	0-40	44	35 (20.5-99.5)
AST, median (IQR)	0-40	44	49.5 (31.5-92.5)
LDH, median (IQR)	240-480	44	662.5 (564-873)

Table 1. Main baseline features of the 44 patients enrolled. All but 4 patients received high-dose GC at diagnosis, associated with methotrexate and IVIG in 63.6% and 20.5%, respectively.

IQR = Interquartile Range; SD = Standard Deviation; VAS = Visual Analog Scale.

RESULTS

Figure 1. Time to skin remission (N=41, 3 patients with no signs of skin involvement at baseline were excluded).
Skin remission in **82.93%**
Median time: ***11.97 months*** (95%CI:6.67-18.64)

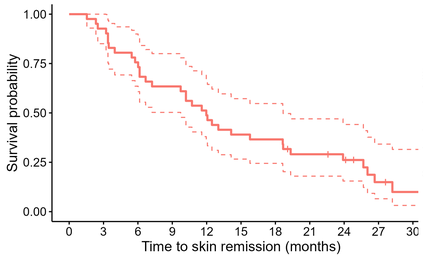


Figure 2. Time to muscle remission (N=38, 6 patients with no signs of muscle involvement at baseline were excluded).
Muscle remission in **94.74%**
Median time: ***5.57 months*** (95%CI:3.29-8.25)

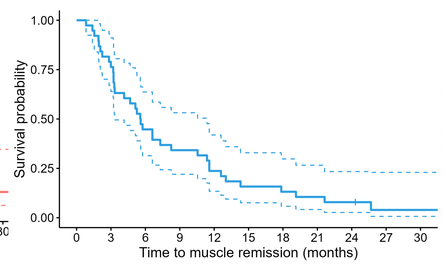


Figure 3. Time to normalisation of muscle enzymes
(N=34, 10 patients with normal muscle enzymes at baseline were excluded).
Normalization of muscle enzymes in **94.12%**
Median time: ***2.99 months*** (95%CI:2.20-5.06)

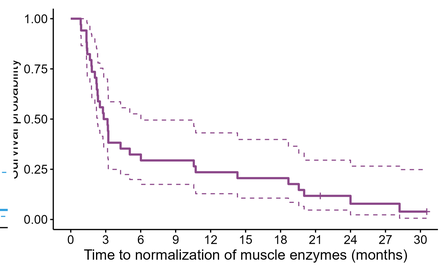


Figure 4. Time to inactive disease according to PRINTO modified criteria*.
Inactive disease according to PRINTO modified criteria in **79.54%** Median time: ***12.97 months*** (95%CI: 11.37-21.63)
*Modified PRINTO criteria for inactive disease: PhGA<=0.2, and at least 2 of 3: i) CK<=150, ii) CMAS>=48, iii) MMT8>=78

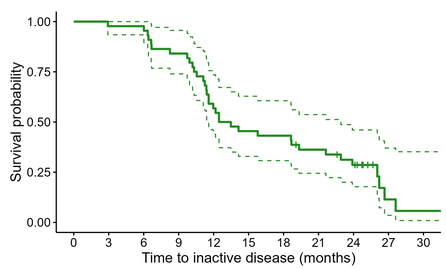


Figure 5. Time to steroid discontinuation
(N=41, 3 patients without CS therapy at baseline were excluded).
Steroid discontinuation in **34.15%**
Median time was not reached (95% CI: 21.80–not reached)

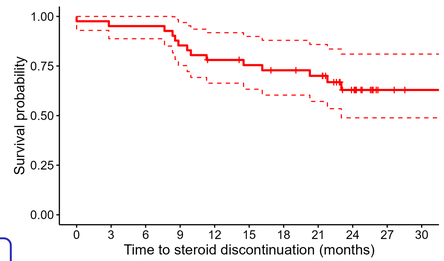


Figure 6. Time to reach steroid dose <0.3 mg/kg/day
(N=40, 3 patients without CS therapy at baseline and 1 patient with steroid dose at baseline <0.3 were excluded).
The **proportion of patients who reached a steroid dose <0.3 mg/kg/day** was ***100%***
Median time: ***11.24 months*** (95% CI: 6.46–12.06).

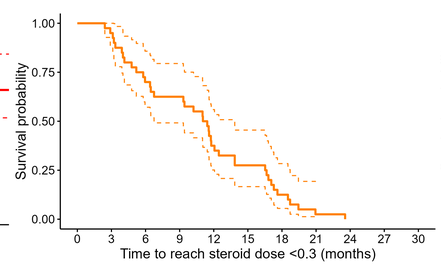


Figure 7. Time to reach steroid dose <0.1 mg/kg/day
(N=41, 3 patients without CS therapy at baseline were excluded).
The **proportion of patients who reached a steroid dose <0.1 mg/kg/day** was **56.10%**
Median time: ***24.73 months*** (95% CI: 19.26–25.81)

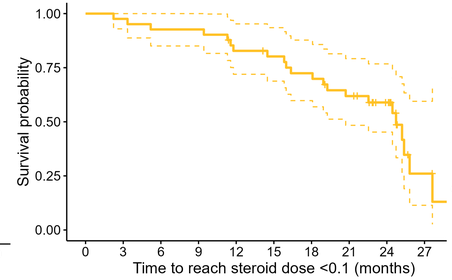
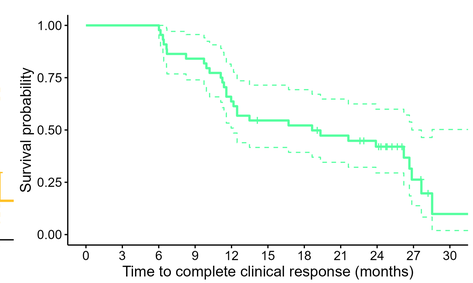


Figure 8. Time to complete clinical response.
·oportion of patients who achieved complete clinical response was ***68.18%***
Median time: ***18.64 months*** (95%CI: 11.57-26.66)



- Only 1 patient (***2.27%***) achieved **remission off therapy** after *28.21 months*.
- 37/44 patients (***84.09%***) achieved at least the **minimal IMACS treatment response**, 30/44 (***68.18%***) patients achieved at least the **moderate IMACS treatment response**, and 18/44 (***40.91%***) patients achieved the **major IMACS treatment response** [median times not shown].
- 25/25 patients (***100%***) achieved at least the **minimal PRINTO treatment response**, 23/25 (***92%***) patients achieved at least the **moderate PRINTO treatment response**, and 13/25 (***52%***) patients achieved the **major PRINTO treatment response** [median times not shown].
- 24/25 patients (***96%***) achieved at least the **JDMAI1/JDMAI2 Low Disease Activity** threshold [median time not shown], and 22/25 (**88%**) patients achieved the **JDMAI1/JDMAI2 Inactive Disease** threshold [median time ***11.49 months*** (95% CI: 8.38-12.85) and ***10.06 months*** (95% CI: 5.82-12.85), respectively].
- JDMAI1 and JDMAI2 scores declined over time, especially at 12 months (mean absolute/percentage change from baseline: -14.1/-90.0% for JDMAI1, -14.7/-84.4% for JDMAI2).

CONCLUSIONS

Our findings provide preliminary figures derived from the real world of clinical practice that may help to define suitable targets and optimal timing of their achievement for the future introduction of the T2T strategy in JDM.

References: Rosina S, et al. Development and validation of a composite disease activity score for measurement of muscle and skin involvement in juvenile dermatomyositis. Rheumatology (Oxford) 2019;58(7):1196-1205.
Rosina S, et al.; Paediatric Rheumatology International Trials Organisation (PRINTO). Defining criteria for disease activity states in juvenile dermatomyositis based on the Juvenile Dermatomyositis Activity Index. RMD Open 2024;10(1):e003093.

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