

Real-world systemic treatment patterns and outcomes of children with severe alopecia areata: a French nationwide study (ESTAPED Cohort)

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Supplement Text1: Search algorithm

A comprehensive keyword search strategy was applied with the following terms:

“Pelade; alopecia areata; methotrexate; Imeth; metoject; izixate; ledertrexate; metotab; nordimet; novatrex; prexate; bolus de corticoids; methylprednisolone; bolus de prednisone; solumedrol; corticothérapie; cortancyl; cortisone; anti-JAK; inhibiteurs de Janus Kinase; tofacitinib; JAKi; Upadacitinib; ritlecitinib; abrocitinib; baricitinib; ruxolitinib; dupilumab and Dupixent”

Supplement Text2: Dosage range of first-line systemic treatments

For intravenous corticosteroids: 5mg/kg twice a day to 10 mg/kg once a day or 125 mg to 1.5 g per bolus, 3 days per month.

Oral corticosteroids: 0.5 to 1 mg/kg and for pulsed or weekend doses: 8 to 10 mg per administration.

Methotrexate: 5 to 20 mg per week or 0.3 mg/kg per week.

Baricitinib: 2 or 4 mg/day.

Combination of methotrexate and oral corticosteroids: methotrexate 7.5 to 20 mg/week, combined with oral corticosteroids initiated at 0.5–1 mg/kg/day and progressively tapered over several weeks to months.

Combination of methotrexate and intravenous corticosteroids: methotrexate 5 to 25 mg/week, combined with monthly intravenous corticosteroids pulses (5 to 10 mg/kg/day or fixed doses of 150–500 mg) given once or twice daily for 3 consecutive days, over 2 to 6 months.

Supplement Text3: Adverse event

Adverse event for first-line ST were as follows: asthenia in 6.4% (6/94), acne in 2.1% (2/94) and infections in 2.1% (2/94) of patients with IV CS, infections in 14.3% (1/7) patients with baricitinib, asthenia and digestive disorders in 4.3% (1/23) of patients with MTX combined

with oral CS. Oral CS alone were well tolerated, with minimal adverse effects. The combination of MTX + IV CS, as well as MTX alone, resulted in higher adverse effects, including nausea/vomiting (7.9% [5/63] and 3.6% [1/28], respectively), abdominal pain (7.9% [5/63] and 7.1% [2/28], respectively), asthenia (6.3% [4/63] and 10.7% [3/28], respectively) and digestive disorders (4.8% [3/63] and 14.3% [4/28], respectively).

Supplement Text4: Main reasons for discontinuing second-line treatments

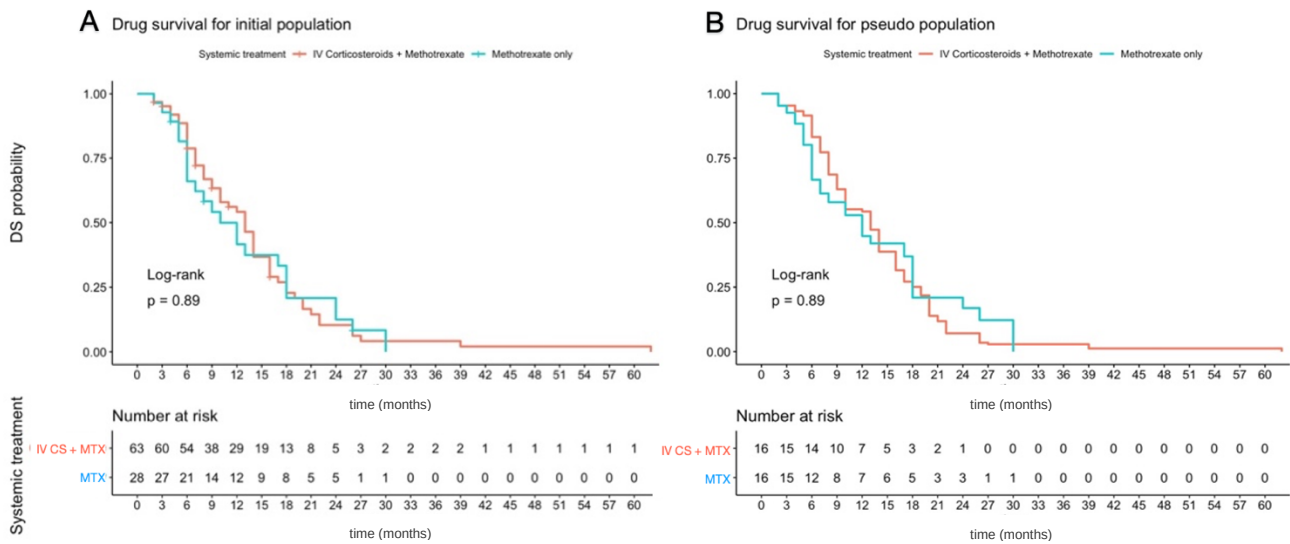
Main reasons for discontinuing second-line treatments were inefficacy, efficacy, and adverse events (or other causes). Inefficacy was the most common reason, reported in 100.0% (n=1) of cases for dupilumab, 75.0% (n=6) for the combination of oral CS and MTX, 70.6% (n=12) for MTX alone, 66.7% (n=2) for baricitinib, 64.3% (n=9) for oral CS, 55.6% (n=10) for IV CS and 55.0% (n=11) for MTX + IV CS. In contrast, 35.7% (n=5) of oral CS, 33.3% (n=6) of IV CS, 33.3% (n=1) for baricitinib, 15% (n=3) for MTX + IV CS, 12.5% (n=1) for MTX + oral CS and 5.8% (n=1) for MTX were discontinued due to efficacy. Discontinuation due to adverse events was observed in 100.0% (n=1) of cases for upadacitinib, 20.0% (n=4) for IV CS combined with MTX, 11.8% (n=2) for MTX alone, and 11.1% (n=2) for IV CS.

Table S1: Reasons of discontinuation of the whole treatment courses during the follow-up

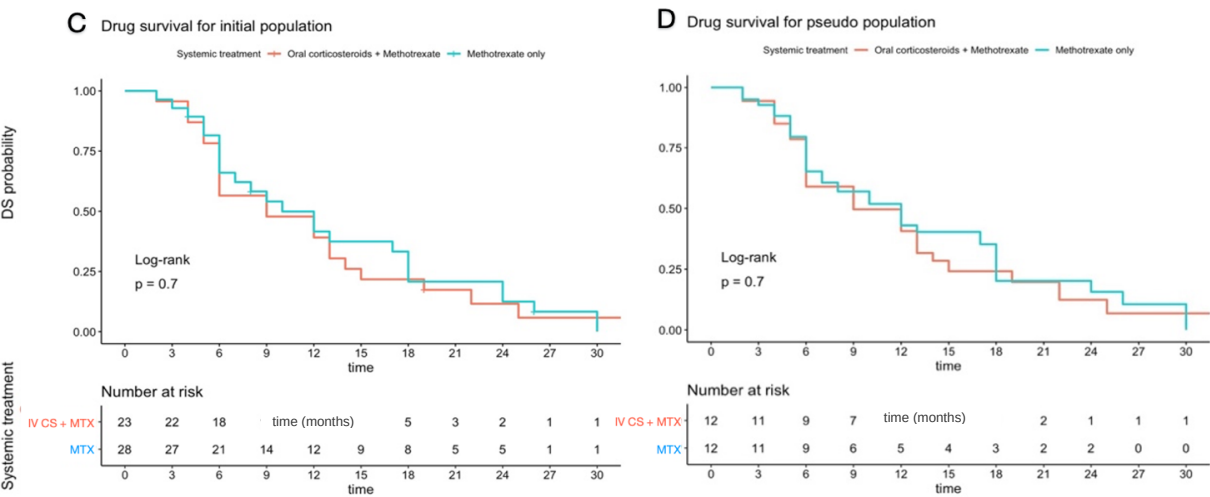
	First-line treatment	Second-line treatment	Third-line treatment	Fourth-line treatment	Fifth-line treatment	Sixth-line treatment
N (%)	243	82	23	7	2	1
Efficacy	84 (34.6)	17 (20.7)	4 (17.4)	0 (0)	1 (50)	1 (100)
Inefficacy	126 (51.9)	51 (62.2)	14 (60.9)	5 (71.4)	1 (50)	0
Adverse event	27 (11.1)	10 (12.2)	1 (4.3)	1 (14.3)	0	0
Other	6 (2.5)	4 (4.9)	4 (17.4)	1 (14.3)	0	0

Figure S1: Kaplan-Meier curves performing within initial population (A and C) pseudo-populations (B and D) with a 2 by 2 comparison (methotrexate=Ref).

Methotrexate and methotrexate associated with intravenous corticosteroids (crude (A) and weighted (B) log-rank test)



Methotrexate and methotrexate associated with oral corticosteroids (crude (C) and weighted (D) log-rank test)



Abbreviations : IV CS intravenous corticosteroids combined with methotrexate ; MTX, methotrexate