2015. Thalidomide kids UC

RCT/Thalidomide/ UC/ Induction

Effect of Thalidomide on Clinical Remission in Children and Adolescents with UC Refractory to Other Immunosuppressives: Pilot Randomized Clinical Trial

Double-blind, placebo-controlled randomized controlled trial.
Patients with refractoy UC were randomized to:
Thalidomide 1.5 to 2.5mg/kg/day or placebo.
In an OLE, non-responders to placebo received thalidomide for 8w.
All responders were followed for 52w.

Primary endpoints: Clinical remission at w8 (PUCAI<10)

Results:

- W8 clinical remission, 83.3% thalidomide vs 18.2% placebo, p=0.005
- Non-responders to placebo, swithed to thalidomide: 72.2% remission w8.
- Clinical remission in thalidomide group 135 weeks vs 8weeks placebo, p<0.0001
- Severe adverse events 3.1/1000 patient-weeks. Peripheral neuropathy and amenorrhea most frequent.

Conclusion:
In this pilot randomized controlled trial on cases of UC refractory to immunosuppressive therapy, thalidomide compared with placebo resulted in improved clinical remission at 8 weeks of treatment and in longer term maintenance of remission. These findings require replication in larger clinical studies evaluating both thalidomide efficacy and safety.

TABLE 2. Efficacy Data

	Randomized to Thalidomide (N = 12)	Randomized to Placebo (N = 11)	Switched to Thalidomide After Placebo Failure (N = 11)	*P*: RCT Phase[a]	*P*: Open-label Phase[b]
Outcomes at week 8					
Clinical remission, N (%)[c]	10 (83.3)	2 (18.2)	8 (72.7)	0.005	0.03
Clinical response, N (%)[c]	8 (83.3)	2 (18.2)	7 (63.6)	0.03	0.04
PUCAI score, mean (CI)	12.9 (−1.4 to 27.3)	33.2 (21.1 to 45.3)	12.3 (5.7 to 18.8)	0.001	0.008
Change in ESR, mean (CI), mm/h	−18.6 (−36.4 to −0.8)	14.4 (5.6 to 23.1)	−22.0 (−34.6 to −9.4)	<0.001	0.003
Change in CRP, mean (CI), mg/dL	−0.2 (−0.9 to 0.6)	0.2 (−0.3 to 0.6)	−0.2 (−0.6 to 0.2)	0.1	0.08
Change in WAZ, mean (CI)	0.50 (0.19 to 0.81)	−0.01 (−0.22 to 0.20)	0.11 (0.01 to 0.21)	<0.001	0.2
Change in BMI z-score, mean (CI)	0.64 (0.24 to 1.04)	0.01 (−0.25 to 0.27)	0.12 (0.01 to 0.24)	<0.001	0.3
Change in physician's global assessment score, mean (CI)[d]	1.7 (1.0 to 2.4)	0.2 (−0.7 to 1.1)	1.6 (0.7 to 2.7)	<0.001	0.02
Steroids[e]					
Mean dose, mean (CI), mg/kg	0.3 (0.3 to 0.3)	0.4 (0.2 to 0.5)	0.3 (0.0 to 0.7)	0.03	0.06
Outcomes at week 4					
Clinical response, N (%)[c]	7 (58.3)	4 (36.3)	5 (45.4)	0.5	0.9
PUCAI score, mean (CI)	20.4 (6.6 to 34.2)	27.3 (15.6 to 38.9)	12.7 (6.1 to 19.4)	0.2	0.06
Change in ESR, mean (CI), mm/h	−15.2 (−34.7 to −4.3)	0.7 (−9.7 to 11.1)	−19.3 (−32.4 to −6.2)	0.02	0.06
Change in CRP, mean (CI), mg/dL	−0.1 (−0.9 to 0.7)	0.2 (−0.4 to 0.7)	−0.2 (−1.0 to 0.6)	0.6	0.2
Change in WAZ, mean (CI)	0.40 (0.09 to 0.71)	−0.01 (−0.19 to 0.17)	0.03 (−0.08 to 0.14)	0.001	0.2
Change in BMI z-score, mean (CI)	0.53 (0.13 to 0.93)	0.01 (−0.20 to 0.22)	0.06 (−0.08 to 0.21)	0.001	0.4
Change in physician's global assessment score, mean (CI)[d]	0.7 (−0.5 to 1.9)	0.9 (−0.2 to 2.0)	1.5 (0.7 to 2.2)	0.6	0.2
Steroids					
Mean dose, mean (CI), mg/kg	0.6 (0.2 to 0.9)	0.4 (0.1 to 0.6)	0.5 (0.1 to 0.8)	0.6	0.2

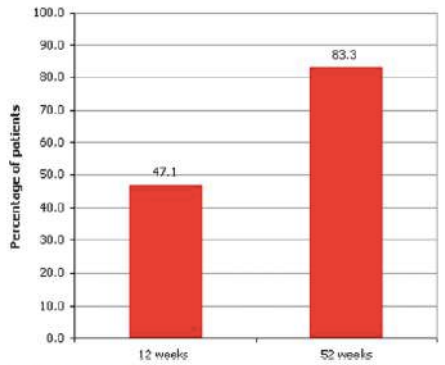

FIGURE 4. Mucosal healing. The graph depicts the percentage of responders to thalidomide reaching mucosal healing at weeks 12 and 52.

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