



EVALUATION OF COMBINATION THERAPY WITH ETANERCEPT AND SYSTEMIC CORTICOSTEROIDS FOR STEVENS-JOHNSON SYNDROME AND TOXIC EPIDERMAL NECROLYSIS: A MULTICENTER OBSERVATIONAL STUDY

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INTRODUCTION

- Treatment of Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) is controversial
 - Corticosteroids
 - Most common worldwide
 - High mortality rates
 - Intravenous immunoglobulins
 - Potential to suppress type IV hypersensitivity and cell apoptosis
 - Questionable efficacy, high cost
 - Tumor necrosis factor-alpha (TNF- α) inhibitors
 - T-cells secrete TNF- α \rightarrow cell death
 - Recent cases of success
 - Combination therapy
 - Common in other disorders
 - Enhanced efficacy, decreased adverse effects
- **Study Aim:** Evaluate the effectiveness of combination therapy with a TNF- α inhibitor and corticosteroid for the treatment of SJS-TEN

METHODS

- Multicenter, retrospective analysis from 2014-2019 in mainland China and Taiwan
- Data Collected
 - SJS-TEN diagnosis based on the Registry of Severe Cutaneous Adverse Reaction (RegiSCAR) criteria
 - Patient demographics, SCORTEN score, average corticosteroid dose, observed mortality rate, standardized mortality rate, adverse events, and several others
- Demographics
 - 242 patients enrolled
 - Corticosteroid monotherapy: 196 (81%)
 - TNF- α inhibitor (etanercept) + corticosteroid: 25 (10.3%)
 - IVIG + corticosteroid: 21 (8.7%)

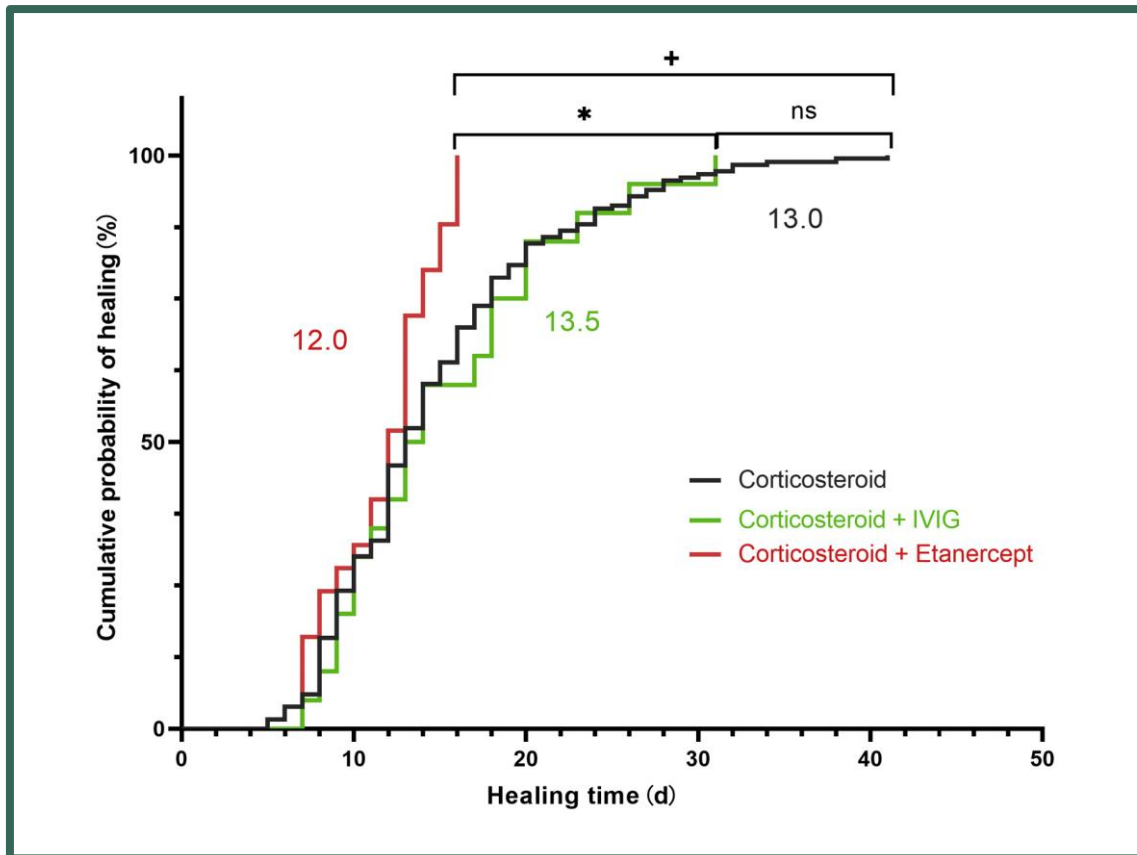
DEMOGRAPHICS

Characteristic	All (n = 242)	Corticosteroids (n = 196)	Corticosteroids with IVIG (n = 21)	Corticosteroids with etanercept (n = 25)	P value
Age, y, mean ± SD	51.13 ± 21.96	52.13 ± 22.17	44.02 ± 19.88	49.24 ± 21.48	.248 *
Sex, n (%)					.100 ‡
Male	122 (50.4)	101 (51.5)	13 (61.9)	8 (32.0)	
Female	120 (49.6)	95 (48.5)	8 (38.1)	17 (68.0)	
Comorbid malignancy, n (%)					.001 ††
+	16 (6.6)	8 (4.1)	1 (4.8)	7 (28.0)	
-	226 (93.4)	188 (95.9)	20 (95.2)	18 (72.0)	
TBSA% (blister or epidermal detachment), mean ± SD	22.93 ± 25.31	19.94 ± 23.07	35.95 ± 33.38	35.40 ± 28.22	.001 * † §
Skin detachment, n (%)					.019 ††
TBSA > 10%	126 (52.1)	94 (48.0)	13 (61.9)	19 (76.0)	
TBSA ≤ 10%	116 (47.9)	102 (52.0)	8 (38.1)	6 (24.0)	
SCORTEN, mean ± SD	1.03 ± 1.27	0.86 ± 1.26	1.81 ± 1.08	1.68 ± 1.07	<.001 * † §
BUN, mmol/L, mean ± SD ‖	15.42 ± 21.15	16.65 ± 20.23	6.59 ± 3.13	13.23 ± 32.74	.100 *
GOT, KU/mL, mean ± SD ¶	59.35 ± 91.26	61.41 ± 99.58	52.00 ± 36.93	49.36 ± 41.59	.766 *
GPT, KU/mL, mean ± SD ¶	54.24 ± 95.80	57.60 ± 105.12	32.95 ± 21.11	45.80 ± 37.92	.481 *
Eosinophil counts, %, mean ± SD #	1.27 ± 2.37	1.36 ± 2.50	0.20 ± 0.30	1.43 ± 2.07	.096 *
WBC × 10 ⁹ /L, mean ± SD **	8.21 ± 4.88	8.62 ± 5.16	6.70 ± 2.26	6.25 ± 3.30	.023 *
Average dosage of corticosteroid (methylprednisolone), mg/kg/d, mean ± SD	1.93 ± 12.08	2.07 ± 13.43	1.47 ± 0.41	1.22 ± 0.52	.932 *

* Indicates that there was a statistical significance between monotherapy with corticosteroids treatment, and combination of corticosteroids and etanercept treatment groups.

§ Indicates that there was a statistically significant difference between the corticosteroids monotherapy, and combination of corticosteroids and IVIG treatment groups.

RESULTS



- Complete skin healing time
 - Corticosteroid 13.0 days (IQR 10.0-18.0)
 - IVIG + corticosteroid 13.5 days (IQR 10.0-19.5)
 - Etanercept + corticosteroid 12.0 days (IQR 8.5-14.0)
 - Statistically significant (p= 0.004, 0.012 respectively)
- Complete skin healing by severity
 - Severe phenotype TEN
 - Corticosteroid 18.5 days (IQR 12.0-26.5)
 - IVIG + corticosteroid 15.5 days (IQR 10.8-21.5)
 - TNF-a + corticosteroid 12.5 days (IQR 9.3-14.0)
 - Statistically significant (p<0.001, 0.026 respectively)
 - Mild – moderate skin involvement
 - No statistically significant difference among treatments

MORTALITY RATES

The probabilities of death associated to each SCORTEN score		Corticosteroids			Corticosteroids with IVIG			Corticosteroids with etanercept			P-value
SCORTEN	Expected mortality, %	Patients (n)	Expected deaths	Observed deaths	Patients (n)	Expected deaths	Observed deaths	Patients (n)	Expected deaths	Observed deaths	
0	3.2	102	3.26	0	2	0.06	0	3	0.1	0	
1	3.2	57	1.82	2	7	0.22	0	9	0.29	0	
2	12.1	19	2.3	3	6	0.73	1	7	0.85	0	
3	35.3	5	1.76	1	5	1.77	0	5	1.77	0	
4	58.3	8	4.66	3	1	0.58	0	1	0.58	0	
≥5	90	5	4.5	4	0	0	0	0	0	0	
Total		196	18.3	13	21	3.36	1	25	3.59	0	
Expected predicted mortality rates, %		9.34 (18.30 of 196)			16.00 (3.36 of 21)			14.36 (3.59 of 25)			0.395
Actual mortality rates, %		6.63 (13 of 196)			4.76 (1 of 21)			0 (0 of 25)			0.504
Standardized mortality rate		0.71 (13 of 18.3) (95% CI 0.83–2.64)			0.30 (1 of 3.36)(95% CI 0.68–6.22)			0 (0 of 3.59) (95% CI 1.80-3.59)			0.006

ADVERSE EVENTS

Adverse Events	SJS or SJS-TEN overlapping (n = 187)							TEN (n = 55)						
	Corticosteroids (n = 164)		Corticosteroids with IVIG (n = 10)		Corticosteroids with etanercept (n = 13)		P-value	Corticosteroids (n = 32)		Corticosteroids with IVIG (n = 11)		Corticosteroids with etanercept (n = 12)		P-value
	n	%	n	%	n	%		n	%	n	%	n	%	
Hypertension							0.53							0.125
+	22	13.4	0	0	2	15.4		6	18.8	0	0	4	33.3	
-	142	86.6	10	100	11	84.6		26	81.3	11	100	8	66.7	
Hyperglycemia							0.811							0.898
+	13	7.9	0	0	0	0		6	18.8	2	18.2	3	25	
-	151	92.1	10	100	13	100		26	81.3	9	81.8	9	75	
GI hemorrhage (grade 2)							0.0021							<.001
+	48	29.3	1	10	0	0		18	56.3	1	9.1	0	0	
-	116	70.7	9	90	13	100		14	43.7	10	90.9	12	100	

RESULTS SUMMARY

- When compared to SJS-TEN patients treated with corticosteroid monotherapy, patients treated with etanercept + corticosteroids:
 - Increased baseline SCORTEN scores
 - Decreased mortality rates
 - Decreased skin healing time
 - Decreased rate of GI hemorrhage

DISCUSSION

- Limitations
 - Small number of IVIG and etanercept cases
 - Asian population → limited generalization
 - Few centers involved → results may reflect local conditions in treating centers
- Future Direction
 - Larger, randomized controlled trials to investigate efficacy of combination therapies

QUESTIONS

