11.4 Efficacy Results and Tabulations of Individual Patient Data

11.4.1 Analysis of Efficacy

The primary endpoint was the elapsed time from skin graft donor site harvest and treatment application to cessation of bleeding (time to reach hemostasis).

11.4.1.1 *Hemostasis*

The mean (SD) and median bleeding times were 3.53 (2.15) min and 3.00 min (Q1, Q3: 2.00, 3.00), respectively, for those subjects treated with TT-173. Those times were significantly shorter ($p<0.0001$) than in the placebo group, in which the mean (SD) and median times were, respectively, 6.73 (2.80) min and 7.00 min (Q1, Q3: 4.00, 10.00).

To gain further information, bleeding times were further analyzed, from 1:00 min to 10:00 min, according to the minute in which haemostasis was reached, and compared between both study treatment arms. Overall, haemostasis was reached before in the subjects treated with TT-173 and the comparison between TT-173 and placebo was also statistically significant ($p=0.0012$) (Table 5 and Figure 2).

Haemostasis was reached within 1.00 to 4.00 min in most of the subjects (73.68%, 28 out of 38) treated with TT-173. By contrast, in the subjects treated with placebo, haemostasis was reached from 5.00 to 10.00 min (66.66%, 22 out of 33). In addition, haemostasis was reached within the first minute in 18.42% (7 out of 38) of the subjects treated with TT-173, while bleeding persisted during the first minute in all the subjects treated with placebo. Moreover, bleeding stopped within the first 3 minutes in 55.26% (21 out of 38) of the subjects who received TT-173, but only in 15.15% (5 out of 33) of those who received placebo. Overall, bleeding lasted less than 10 min in all subjects treated with TT-173, while in 27.27% (9 out of 33) of the subjects treated with placebo haemostasis was reached after 10 minutes.

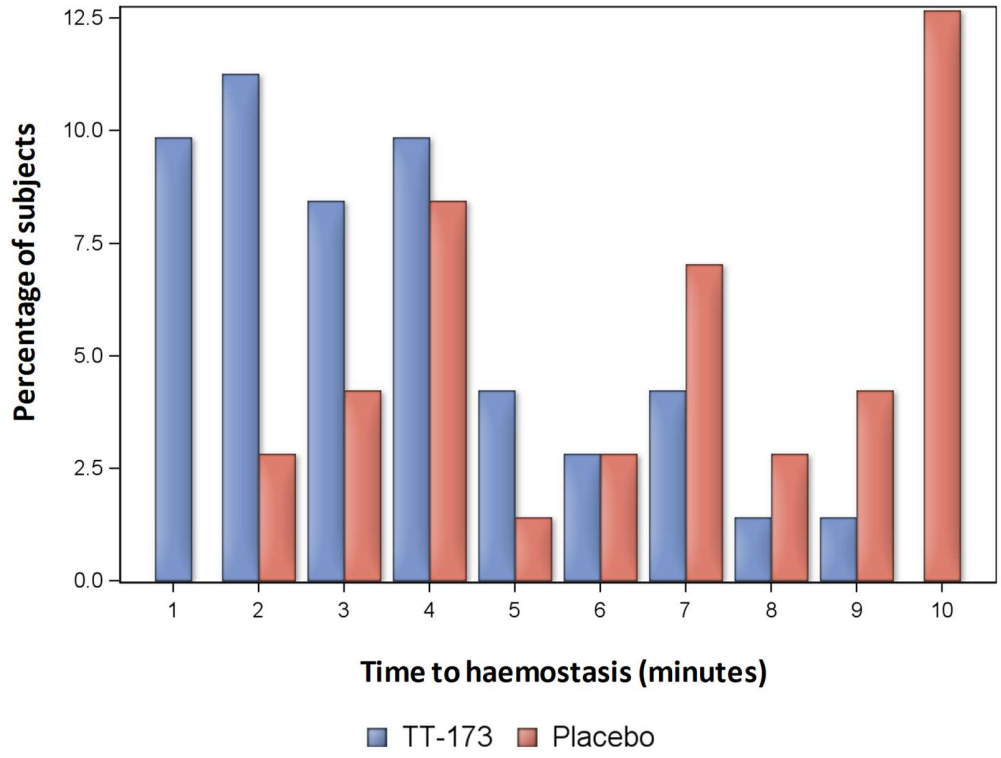
Furthermore, no subjects treated with TT-173 required rescue treatment when 10 minutes from the first treatment dose had elapsed. However, 24.24% (8 out of 33) of the subjects treated with placebo required rescue treatment ($p=0.0013$).

Table 5. Haemostasis time (mITT population)

Time to hemostasis (minutes)	TT-173 (N=38)	Placebo (N=33)	P Value Test
1:00, n (%)	7 (18.42)	0 (0.00)	Fisher: 0.0012

Time to hemostasis (minutes)	TT-173 (N=38)	Placebo (N=33)	P Value Test
2:00, n (%)	8 (21.05)	2 (6.06)	
3:00, n (%)	6 (15.79)	3 (9.09)	
4:00, n (%)	7 (18.42)	6 (18.18)	
5:00, n (%)	3 (7.89)	1 (3.03)	
6:00, n (%)	2 (5.26)	2 (6.06)	
7:00, n (%)	3 (7.89)	5 (15.15)	
8:00, n (%)	1 (2.63)	2 (6.06)	
9:00, n (%)	1 (2.63)	3 (9.09)	
10:00, n (%)	0 (0.00)	9 (27.27)	

Figure 2. Time to haemostasis per treatment arm (mITT population)



Because the subject 0714, treated with placebo, was included in the study but did not fulfill the study eligibility criteria (Section 10.2), the primary endpoint was also analyzed in the mITT

population, but excluding the subject 0714. The results were very similar to those from the full mITT population as mean (SD) and median bleeding times were 3.53 (2.15) min and 3.00 min (Q1, Q3: 2.00, 3.00), respectively, for those subjects treated with TT-173, and 6.69 (2.83) min and 7.00 min (Q1, Q3: 4.00, 10.00) for the subjects treated with placebo.

It was gained further information through a Kaplan-Meier analysis (Figure 3) which showed a statistically significant increased haemostasis probability for the subjects treated with TT-173 compared to the subjects treated with placebo, as the median times to haemostasis from this Kaplan-Meier analysis were 3.0 minutes (95% CI: 2.0 to 4.0) and 7.0 minutes (95% CI: 4.0 to 9.0) in the subjects treated with TT-173 and placebo, respectively; and the hazard ratio (HR) was 0.308 (95%CI: 0.179 to 0.530; log-rank<0.0001).

Figure 3. Time to haemostasis Kaplan-Meier analysis