康龙化成
PHARMARON

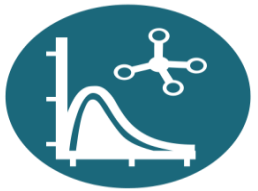

Laboratory Chemistry


Biosciences


Chemistry, Manufacturing and Control


Safety Assessment


Clinical Support


Radiolabelled Sciences

Immuron IMM-124E-2002:
Investigational Product: Travelan*; ETEC strain: H10407

Primary objective: Protection against moderate-severe diarrhea

Secondary objective: Safety, Clinical endpoints,

BACKground

- Travelan® (IMM-124E) is produced from the colostrum of birthing cattle that have been immunised during pregnancy with the outer coat of multiple human enterotoxigenic E.coli (ETEC) known to cause Travelers diarrhea (TD)
- Travelan was first registered in Australia in 2004 as a Therapeutic Goods Administration (TGA) listed medicine and an over the counter product indicated to reduce the risk of TD (AUST L 106709)
- In Canada Travelan was licensed in 2013 as a natural health product (NPN 80046016) indicated to reduce the risk of TD
- In the US Travelan has been marketed as a dietary supplement for digestive tract protection since 2015

immuron

MANUFACTURING

Vaccines

- Proprietary vaccines constituted of cell surface antigens preparations of 13 ETEC strains
- Approved for use in food-producing animals with the Australian Pesticides and Veterinary Medicines Authority (APVMA) after a formal risk assessment
- Manufactured under Good Manufacturing Practice (GMP) in a facility licensed by the APVMA

Colostrum

- Colostrum is collected from cattle on dairy farms using GMP-compliant collection and manufacturing methods. These procedures are within the guidelines of the FDA
- Processing includes pasteurization, separation of fat, ultrafiltration to reduce lactose and concentrate the product, and spray-drying to produce a stable powder that is then milled to 100 microns
- No chemical additives are used in the manufacturing process
- Product is tested under Codex Alimentarius (and U.S.A. FDA) for human consumption

All Enrolled Subjects

	Travelan (n=32)	Placebo (n=31)	Total (n=63)
Randomization	**32**	**31**	**63**
Included in			
Safety Analysis Set	32	31	63
Intent-to-Treat Analysis Set	30	30	60
Completed Study	**27**	**27**	**54**
Discontinued Study	**5**	**4**	**9**
Subject Withdrew Consent	3	3	6
Investigator Discretion	2	0	2
Lost to Follow Up	0	1	1

Summarized table 14.1.1
Note: Intent-to-treat analysis set defined as randomized subjects who received study medication and were challenged.

Summary of Safety

- 3 placebo subjects required IV fluids
- Early Abx treatment: 2/30 IP; 7/30 Placebo
- No SAEs
- All subjects challenged had ETEC negative stool at discharge
- No recrudescence

Summary of Protective Efficacy

Intent-to-treat Analysis Set	**Travelan (N=30)**	**Placebo (N=30)**
Number of subjects with ETEC-induced moderate-severe diarrhea [1]	7 (23.3%)	11 (36.7%)
P-value		0.399
Protective Efficacy (%)		36.4%
95% 2-sided Confidence Interval		(-79.8%, 79.1%)
PE for a 5 Day Period Post Challenge	Travelan (N=30)	Placebo (N=30)
Number of subjects with ETEC-induced moderate-severe diarrhea [1]	6 (20.0%)	10 (33.3%)
P-value		.382
Protective Efficacy (%)		40.0%
95% 2-sided Confidence Interval		(-82.2%, 82.1%)

[1] Defined as >= 4 Grade 3-5 stools in any 24 hour period post-challenge days or >= 401 g of Grade 3-5 stools in any 24 hour period occurring during the post-challenge period

Table 14.3.3.1 Summary of Adverse Events by System Organ Class and Preferred Term - Safety Analysis Set

System Organ Class Preferred Term	Travelan (N = 32) Subjects n (%)	 Events m	Placebo (N = 31) Subjects n (%)	 Events m	Total (N = 63) Subjects n (%)	 Events m
Subjects with at least one AEs	24 (75.0)	58	28 (90.3)	109	52 (82.5)	167
Gastrointestinal disorders	23 (71.9)	43	28 (90.3)	66	51 (81.0)	109
Diarrhoea	18 (56.3)	18	20 (64.5)	22	38 (60.3)	40
Abdominal pain	11 (34.4)	15	13 (41.9)	16	24 (38.1)	31
Nausea	3 (9.4)	3	9 (29.0)	9	12 (19.0)	12
Abdominal distension	3 (9.4)	3	5 (16.1)	5	8 (12.7)	8
Vomiting	2 (6.3)	2	6 (19.4)	6	8 (12.7)	8
Constipation	2 (6.3)	2	3 (9.7)	3	5 (7.9)	5
Haematochezia	0	0	2 (6.5)	2	2 (3.2)	2
Dyspepsia	0	0	1 (3.2)	1	1 (1.6)	1
Flatulence	0	0	1 (3.2)	1	1 (1.6)	1
Toothache	0	0	1 (3.2)	1	1 (1.6)	1

AE = Adverse event; N = Number of subjects in respective treatment arm in Safety Analysis Set, n = Number of subjects with event, % = n/N*100, m = Number of events.

Adverse events are coded with MedDRA version 25.1.

Subjects with multiple occurrences of adverse events in the same preferred term are counted only once within that preferred term.

Subjects with multiple occurrences of adverse events in the same system organ class are counted only once within that system organ class.

System organ class are listed in descending order of frequency and preferred terms are listed in descending order of frequency within system organ class.

Source Data: Listing 16.2.7.1

ADVERSE EVENTS: IP v PLACEBO

cumulative AEs p <.05

	Subjects with AEs	Subjects with no AEs	# of AEs
Group 1 (Travelan)	24	8	58
Group 2 (Placebo)	28	3	109