AceticA Basic Results Summary

ISRCTN11636684 https://doi.org/10.1186/ISRCTN11636684

Participant Flow

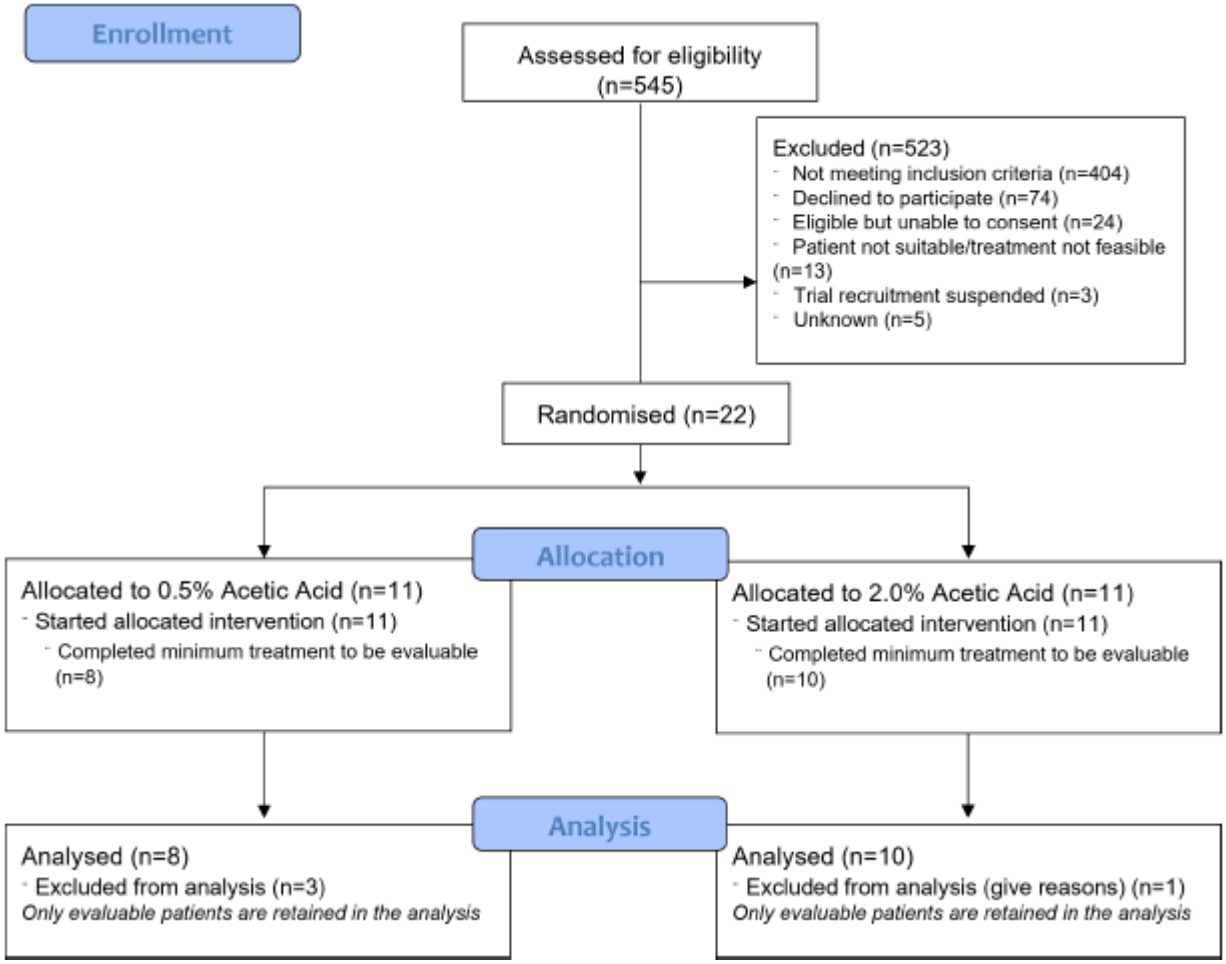

Figure 1. CONSORT diagram

Baseline Characteristics

Table 1: Summary baseline characteristics for all evaluable patients, presented both stratified according to allocated treatment and pooled over the evaluable population.

	Acetic Acid 0.5% (N = 8)	Acetic Acid 2.0% (N=10)	All Evaluable Patients (N=18)
Age at Randomisation (years)			
n	8	10	18
Mean (sd)	44 (12.39)	59.4 (19.57)	52.56 (18.11)
Median (IQR)	44 (37.25, 49.5)	66 (48.75, 73.75)	52 (38.75, 68.25)
Range	(24, 63)	(21, 79)	(21, 79)
Sex (n(%))			
Female	4 (50.00%)	4 (40.00%)	8 (44.44%)
Male	4 (50.00%)	6 (60.00%)	10 (55.56%)
Number of burns per person (n(%))			
1	7 (87.50%)	7 (70.00%)	14 (77.78%)
2	1 (12.50%)	2 (20.00%)	3 (16.67%)
3	0 (0.00%)	1 (10.00%)	1 (5.56%)
Mechanism of injury (n(%))			
Flame	3 (37.50%)	3 (30.00%)	6 (33.33%)
Flash	1 (12.50%)	0 (0.00%)	1 (5.56%)
Scald	4 (50.00%)	7 (70.00%)	11 (61.11%)
Time from burn injury to randomisation (days)			
n	8	10	18
Mean (sd)	12 (11.87)	12.5 (10.41)	12.28 (10.74)
Median (IQR)	7 (3, 16.75)	9 (8.25, 13)	9 (3.5, 14.75)
Range	(3, 36)	(2, 36)	(2, 36)
Location of burn injury* (n(%))			
Buttocks	0 (0.00%)	1 (7.14%)	1 (4.35%)
dorsum left foot	0 (0.00%)	1 (7.14%)	1 (4.35%)
Left Arm	1 (11.11%)	0 (0.00%)	1 (4.35%)
Left leg	1 (11.11%)	5 (35.71%)	6 (26.09%)
Missing	4 (44.44%)	2 (14.29%)	6 (26.09%)
Post. Trunk	0 (0.00%)	1 (7.14%)	1 (4.35%)
Right Arm	1 (11.11%)	2 (14.29%)	3 (13.04%)
right back/ flank	1 (11.11%)	0 (0.00%)	1 (4.35%)
Right leg	1 (11.11%)	2 (14.29%)	3 (13.04%)
Total % Partial Thickness			
n	8	10	18
Mean (sd)	3.86 (3.66)	5.97 (6.17)	5.04 (5.18)
Median (IQR)	3.25 (0.88, 5.55)	3.38 (1.19, 10.19)	3.38 (1, 9.38)
Range	(0, 9.5)	(0, 18)	(0, 18)
Total % Full Thickness			
n	8	9	17
Mean (sd)	10.88 (21.21)	2.5 (3.04)	6.44 (14.84)
Median (IQR)	1.75 (0, 9.38)	1 (0, 4)	1.5 (0, 5)
Range	(0, 62)	(0, 9)	(0, 62)
Total Body Surface Area			
n	8	10	18
Mean (sd)	14.74 (20.48)	8.22 (7.36)	11.12 (14.58)
Median (IQR)	6.95 (2.88, 17)	6.62 (1.94, 12.88)	6.95 (2.5, 14.69)
Range	(1.5, 63)	(1, 22)	(1, 63)

Outcome Measures

Primary outcome measure

To assess efficacy by measuring the bacterial load from microbiology wound swabs taken daily from recruitment for 3 consecutive days.

Table 2: Summary of bacterial load (org/mL) by treatment allocation and sample time point for all burns wounds within evaluable patient population.

Sample Time Point		Acetic Acid 0.5% (N=9 wounds within 8 patients)	Acetic Acid 2.0% (N=14 wounds within 10 patients)	Total (N=23 wounds within 18 patients)
Screening	n	6	9	15
	Mean (sd)	220682.72 (528773.37)	345088.63 (801878.17)	295326.27 (686491.69)
	Median (IQR)	6681.66 (1208.33, 10157.5)	5500 (2300, 10600)	5500 (1740, 10550)
	Range	(33, 1300000)	(117.7, 2400000)	(33, 2400000)
Day 1	n	8	12	20
	Mean (sd)	1444792.91 (4062939.91)	75190.99 (124851.92)	623031.76 (2562150.8)
	Median (IQR)	5 (0, 26083.32)	2618.3 (11.73, 95000)	235.8 (2.25, 41499.98)
	Range	(0, 11500000)	(0, 350000)	(0, 11500000)
Day 2	n	8	13	21
	Mean (sd)	531509.11 (994447.97)	581.28 (1140.82)	202839.5 (644922.54)
	Median (IQR)	234.8 (0, 463702.48)	0 (0, 196.6)	0 (0, 1603.3)
	Range	(0, 2400000)	(0, 3700)	(0, 2400000)
Day 3	n	8	13	21
	Mean (sd)	97523.75 (110429.67)	5633.33 (19941.96)	40639.2 (81225.71)
	Median (IQR)	67595 (0, 180000)	0 (0, 43.3)	0 (0, 690)
	Range	(0, 245000)	(0, 72000)	(0, 245000)
Day 4	n	8	13	21
	Mean (sd)	393262.5 (691796.09)	5441.02 (19102.86)	153182.54 (452731.55)
	Median (IQR)	50050 (0, 461500)	0 (0, 0)	0 (0, 1700)
	Range	(0, 2000000)	(0, 69000)	(0, 2000000)

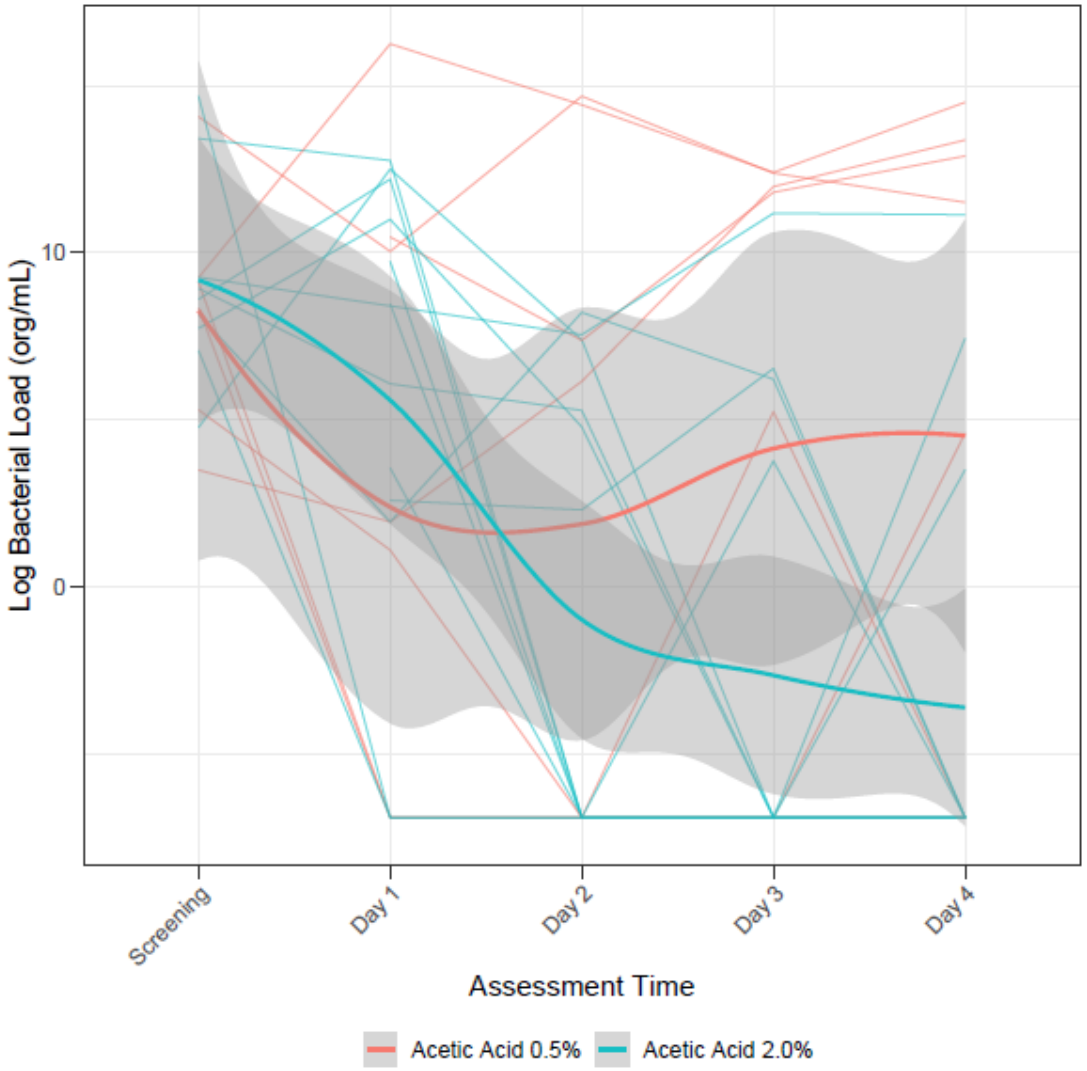

Figure 2. Repeated measures plot of Bacterial Load (org/mL) over assessment days for evaluable patients in the AceticA Trial. Individual wound within patient lines are shown in the background and loess smoothed trend lines added to aid interpretation of treatment allocation trends. The colour of the line indicates the treatment allocation.

Secondary outcome measures

1. **The antimicrobial activity of acetic acid will be measured by extracting fluid from removed burns dressings and assessing the minimum inhibitory concentrations (MIC) to establish if active acetic acid is still present.**

Antimicrobial activity of acetic acid was measured by extracting fluid removed from burns dressings. The MIC was estimated by successively halving the concentration of retrieved acid and testing whether microbial growth occurs. Each dressing assessment yielded the number of dilutions that occurred before inhibitory behaviour was lost.

Results of MIC ascertainment was only provided on three occasions, all of which were returned as either insufficient retrieved acid, or that the sample was not received. Therefore, there are no results to summarise.

2. Tolerance will be assessed by measuring a patient's pain scores with a Visual Analogue Scale (VAS) if the patient has capacity to provide scores.

Table 3: Summary of tolerance scored by treatment allocation and sample timepoint for burns wounds within patients in the evaluable population.

Sample Time Point		Acetic Acid 0.5% (N=8 wounds within 8 patients)	Acetic Acid 2.0% (N=12 wounds within 10 patients)
Day 1 AM, pre analgesia for dressing change	No pain	0 (0%)	3 (25%)
	Mild pain	3 (37.5%)	4 (33.33%)
	Moderate pain	2 (25%)	0 (0%)
	Severe pain	0 (0%)	2 (16.67%)
	Very severe pain	1 (12.5%)	3 (25%)
	Not assessed	2 (25%)	0 (0%)
Day 1 AM, post burn injury clean and pre-dressing change	No pain	0 (0%)	0 (0%)
	Mild pain	1 (12.5%)	3 (25%)
	Moderate pain	2 (25%)	0 (0%)
	Severe pain	0 (0%)	1 (8.33%)
	Very severe pain	0 (0%)	1 (8.33%)
	Not assessed	5 (62.5%)	7 (58.33%)
Day 1 AM, immediately post new dressing application	No pain	2 (25%)	0 (0%)
	Mild pain	1 (12.5%)	0 (0%)
	Moderate pain	0 (0%)	1 (8.33%)
	Severe pain	0 (0%)	4 (33.33%)
	Very severe pain	0 (0%)	0 (0%)
	Not assessed	5 (62.5%)	7 (58.33%)
Day 1 AM, 30 minute post new dressing application	No pain	1 (12.5%)	0 (0%)
	Mild pain	1 (12.5%)	1 (8.33%)
	Moderate pain	1 (12.5%)	3 (25%)
	Severe pain	0 (0%)	1 (8.33%)
	Very severe pain	0 (0%)	0 (0%)
	Not assessed	5 (62.5%)	7 (58.33%)
Day 1 PM, pre analgesia for dressing change	No pain	0 (0%)	5 (41.67%)
	Mild pain	1 (12.5%)	0 (0%)
	Moderate pain	2 (25%)	3 (25%)
	Severe pain	2 (25%)	4 (33.33%)
	Very severe pain	1 (12.5%)	0 (0%)
	Not assessed	2 (25%)	0 (0%)
Day 1 PM, post burn injury clean and pre-dressing change	No pain	0 (0%)	0 (0%)
	Mild pain	1 (12.5%)	0 (0%)
	Moderate pain	1 (12.5%)	4 (33.33%)
	Severe pain	1 (12.5%)	1 (8.33%)
	Very severe pain	0 (0%)	0 (0%)
	Not assessed	5 (62.5%)	7 (58.33%)
	No pain	1 (12.5%)	0 (0%)
	Mild pain	1 (12.5%)	0 (0%)

Table 3 continued:

Sample Time Point		Acetic Acid 0.5% (N=8 wounds within 8 patients)	Acetic Acid 2.0% (N=12 wounds within 10 patients)
Day 1 PM, immediately post new dressing application	Moderate pain	0 (0%)	5 (41.67%)
	Severe pain	1 (12.5%)	0 (0%)
	Very severe pain	0 (0%)	0 (0%)
	Not assessed	5 (62.5%)	7 (58.33%)
Day 1 PM, 30 minute post new dressing application	No pain	0 (0%)	0 (0%)
	Mild pain	2 (25%)	1 (8.33%)
	Moderate pain	0 (0%)	1 (8.33%)
	Severe pain	1 (12.5%)	0 (0%)
	Very severe pain	0 (0%)	0 (0%)
	Not assessed	5 (62.5%)	8 (66.67%)
Day 2 AM, pre analgesia for dressing change	No pain	2 (25%)	5 (41.67%)
	Mild pain	0 (0%)	3 (25%)
	Moderate pain	4 (50%)	0 (0%)
	Severe pain	1 (12.5%)	3 (25%)
	Very severe pain	0 (0%)	1 (8.33%)
	Not assessed	1 (12.5%)	0 (0%)
Day 2 AM, post burn injury clean and pre-dressing change	No pain	1 (12.5%)	0 (0%)
	Mild pain	0 (0%)	0 (0%)
	Moderate pain	1 (12.5%)	2 (16.67%)
	Severe pain	1 (12.5%)	0 (0%)
	Very severe pain	0 (0%)	3 (25%)
	Not assessed	5 (62.5%)	7 (58.33%)
Day 2 AM, immediately post new dressing application	No pain	2 (25%)	1 (8.33%)
	Mild pain	0 (0%)	1 (8.33%)
	Moderate pain	0 (0%)	0 (0%)
	Severe pain	1 (12.5%)	3 (25%)
	Very severe pain	0 (0%)	0 (0%)
	Not assessed	5 (62.5%)	7 (58.33%)
Day 2 AM, 30 minute post new dressing application	No pain	1 (12.5%)	1 (8.33%)
	Mild pain	0 (0%)	0 (0%)
	Moderate pain	0 (0%)	1 (8.33%)
	Severe pain	0 (0%)	0 (0%)
	Very severe pain	0 (0%)	3 (25%)
	Not assessed	7 (87.5%)	7 (58.33%)

Table 3 continued:

Sample Time Point		Acetic Acid 0.5% (N=8 wounds within 8 patients)	Acetic Acid 2.0% (N=12 wounds within 10 patients)
Day 2 PM, pre analgesia for dressing change	No pain	1 (12.5%)	4 (33.33%)
	Mild pain	2 (25%)	2 (16.67%)
	Moderate pain	3 (37.5%)	3 (25%)
	Severe pain	0 (0%)	0 (0%)
	Very severe pain	0 (0%)	0 (0%)
	Not assessed	2 (25%)	1 (8.33%)
Day 2 PM, post burn injury clean and pre-dressing change	No pain	0 (0%)	0 (0%)
	Mild pain	1 (12.5%)	0 (0%)
	Moderate pain	1 (12.5%)	2 (16.67%)
	Severe pain	1 (12.5%)	0 (0%)
	Very severe pain	0 (0%)	0 (0%)
	Not assessed	5 (62.5%)	8 (66.67%)
Day 2 PM, immediately post new dressing application	No pain	1 (12.5%)	0 (0%)
	Mild pain	1 (12.5%)	0 (0%)
	Moderate pain	1 (12.5%)	2 (16.67%)
	Severe pain	0 (0%)	0 (0%)
	Very severe pain	0 (0%)	0 (0%)
	Not assessed	5 (62.5%)	8 (66.67%)
Day 2 PM, 30 minute post new dressing application	No pain	1 (12.5%)	0 (0%)
	Mild pain	1 (12.5%)	1 (8.33%)
	Moderate pain	0 (0%)	1 (8.33%)
	Severe pain	0 (0%)	0 (0%)
	Very severe pain	0 (0%)	0 (0%)
	Not assessed	6 (75%)	8 (66.67%)
Day 3 AM, pre analgesia for dressing change	No pain	2 (25%)	4 (33.33%)
	Mild pain	1 (12.5%)	2 (16.67%)
	Moderate pain	3 (37.5%)	1 (8.33%)
	Severe pain	0 (0%)	1 (8.33%)
	Very severe pain	1 (12.5%)	3 (25%)
	Not assessed	1 (12.5%)	1 (8.33%)
	No pain	1 (12.5%)	0 (0%)
	Mild pain	0 (0%)	0 (0%)
	Moderate pain	2 (25%)	1 (8.33%)
	Severe pain	0 (0%)	1 (8.33%)

Table 3 continued:

Sample Time Point		Acetic Acid 0.5% (N=8 wounds within 8 patients)	Acetic Acid 2.0% (N=12 wounds within 10 patients)
Day 3 AM, post burn injury clean and pre-dressing change	Very severe pain	0 (0%)	3 (25%)
	Not assessed	5 (62.5%)	7 (58.33%)
Day 3 AM, immediately post new dressing application	No pain	2 (25%)	0 (0%)
	Mild pain	0 (0%)	0 (0%)
	Moderate pain	1 (12.5%)	1 (8.33%)
	Severe pain	0 (0%)	3 (25%)
	Very severe pain	0 (0%)	1 (8.33%)
	Not assessed	5 (62.5%)	7 (58.33%)
Day 3 AM, 30 minute post new dressing application	No pain	1 (12.5%)	0 (0%)
	Mild pain	1 (12.5%)	0 (0%)
	Moderate pain	1 (12.5%)	2 (16.67%)
	Severe pain	0 (0%)	0 (0%)
	Very severe pain	0 (0%)	0 (0%)
	Not assessed	5 (62.5%)	8 (66.67%)

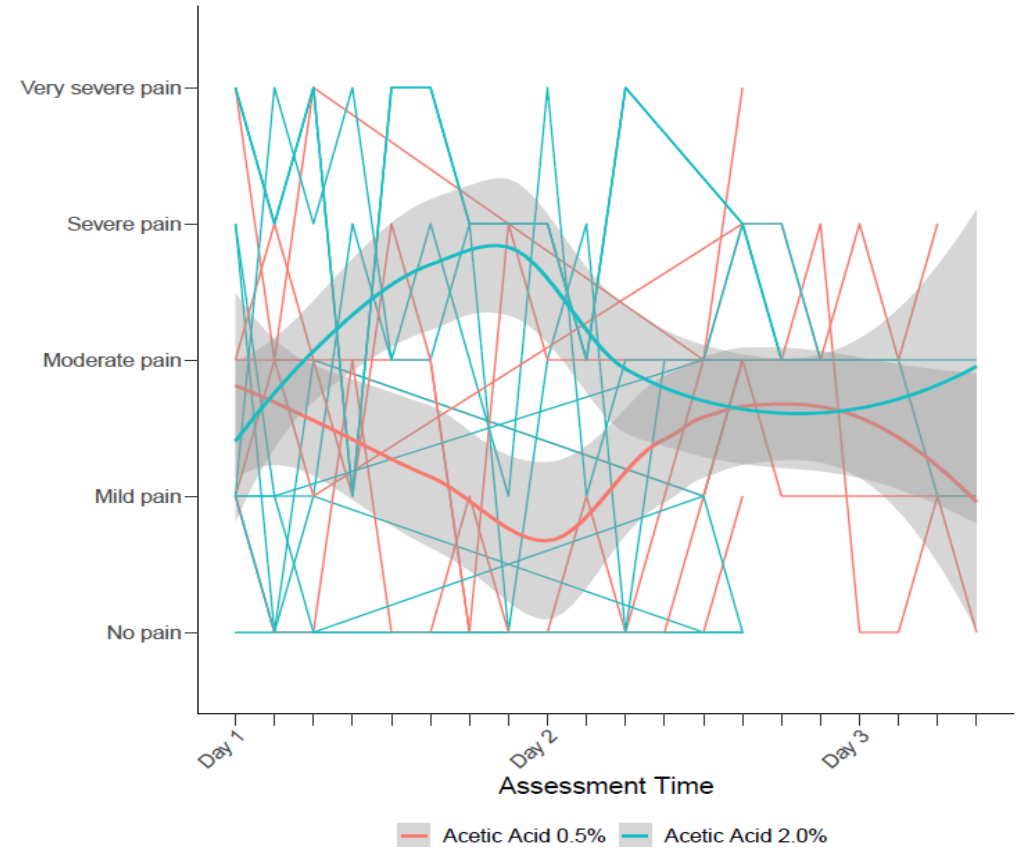

Figure 3. Repeated measures plot of pain scores over assessment days for evaluable patients. Individual wound within patient lines are shown in the background and loess smoothed trend lines added to aid interpretion of treatment allocation trends.

3. Time to 95% wound healing of the treated area of interest.

Table 4: Summary of 95% healing status of individual burns by the end of the AceticA trial, by treatment allocation.

	Acetic Acid 0.5% (N=9 burns within 8 patients)	Acetic Acid 2.0% (N=14 burns within 10 patients)	Total (N=23 burns within 18 patients)
Individual burns 95% healed by end of trial (n(%))			
No	3 (33.33%)	1 (7.14%)	4 (17.39%)
Unknown	3 (33.33%)	7 (50%)	10 (43.48%)
Yes	3 (33.33%)	6 (42.86%)	9 (39.13%)

Table 5: Summary of number of patients with all trial treated burns 95% healed by the end of the AceticA trial, by treatment allocation.

	Acetic Acid 0.5% (N=8)	Acetic Acid 2.0% (N=10)	Total (N=18)
Number of patients with trial treated burns 95% healed by end of trial (n(%))			
No	3 (37.5%)	1 (10%)	4 (22.22%)
Unknown	3 (37.5%)	4 (40%)	7 (38.89%)
Yes	2 (25%)	5 (50%)	7 (38.89%)

4. Perceived treatment allocation, assessed by asking patients after treatment completion which treatment they believed they received if they have capacity to do so.

Table 6: Summary of the number of evaluable patients who completed the AceticA trial by treatment allocation.

	Acetic Acid 0.5% (N=8)	Acetic Acid 2.0% (N=10)	Total (N=18)
Completed treatment (n(%))			
No	2 (25.00%)	0 (0.00%)	2 (11.11%)
Yes	6 (75.00%)	10 (100.00%)	16 (88.89%)

Table 7: Summary of patient perceived treatment allocation of evaluable patients who completed the AceticA trial by treatment allocation.

	Acetic Acid 0.5% (N=6)	Acetic Acid 2.0% (N=10)	Total (N=16)
Patient perceived treatment allocation (n(%))			
0.5% acetic acid	0 (0.00%)	3 (30.00%)	3 (18.75%)
2% acetic acid	2 (33.33%)	0 (0.00%)	2 (12.50%)
Don't know	4 (66.67%)	7 (70.00%)	11 (68.75%)

Adverse Events

Table 8: Summary of the incidence and number of patients affected, by allocated treatment.

	Adverse Event Incidence	Number of Patients Affected
Allocated Treatment		
Acetic Acid 0.5%	6	2
Acetic Acid 2.0%	4	3

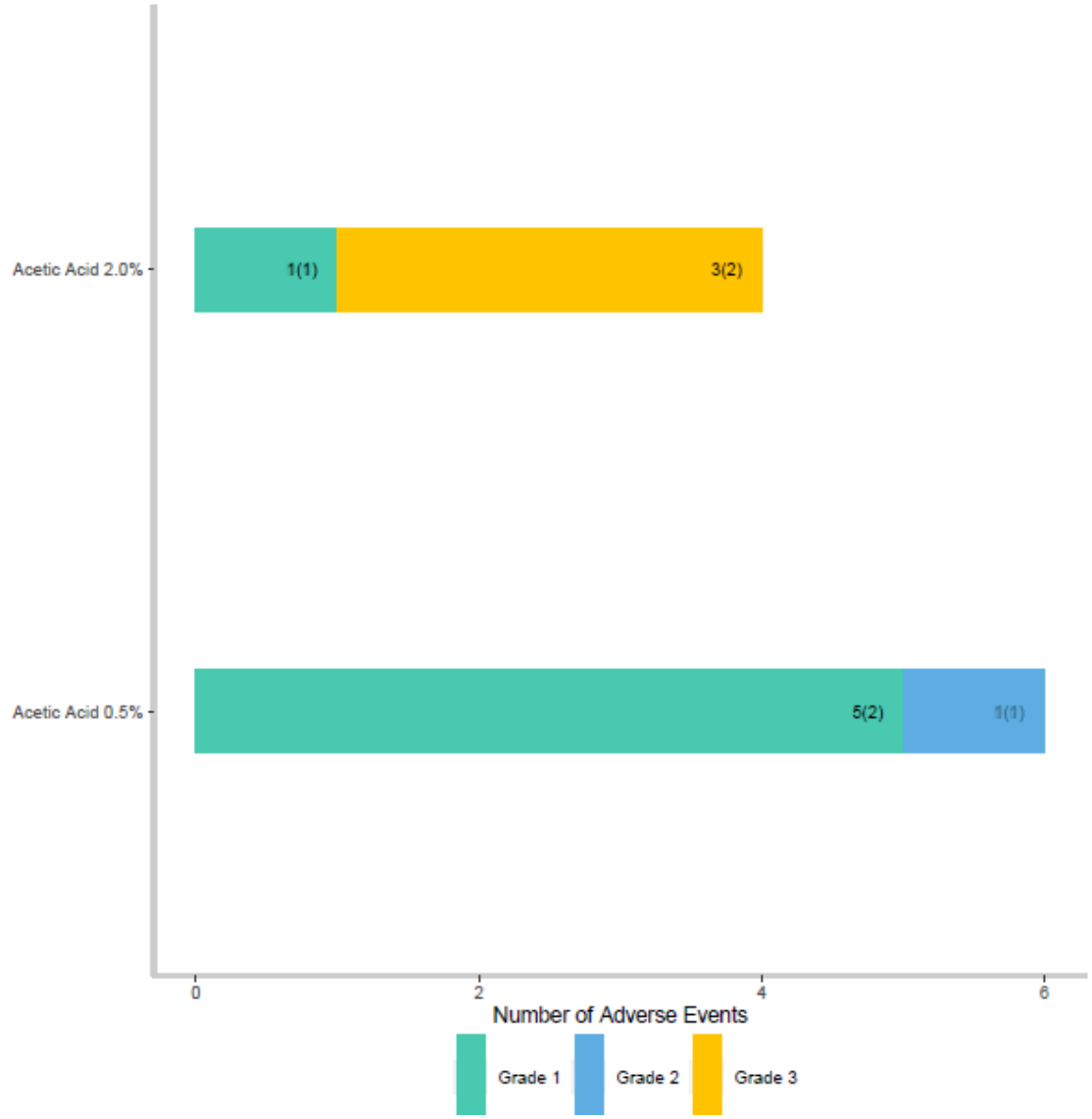

Figure 4: Swimmer plot of the total number of adverse events by CTCAE grade and allocated treatment.

Table 9. Line listing of all AEs reported during the AceticA trial.

Category	Toxicity	Grade	Causality	SAE	Start Date	Time to Onset	Ongoing	Stop Date	Length of AE
Gastrointestinal disorders	Acid reflux	2	Unrelated	No	31-Mar-2018	1	TRUE		
Skin and subcutaneous tissue disorders	Pain	1	Possibly related	No	31-Mar-2018	1	TRUE		
Musculoskeletal and connective tissue disorders	Back pain	1	Unrelated	No	13-Jul-2018	1	TRUE		
Vascular disorders	Leg odema	1	Unrelated	No	13-Jul-2018	1	TRUE		
Gastrointestinal disorders	Nausea	1	Unrelated	No	14-Jul-2018	2	TRUE		
Gastrointestinal disorders	Constipation	1	Unrelated	No	14-Jul-2018	2	TRUE		
Gastrointestinal disorders	Constipation	1	Unlikely to be related	No	10-Mar-2018	-152	TRUE		
Metabolism and nutrition disorders	Hyperglycaemia	3	Unrelated	No	09-Sep-2019	2	TRUE		
Infections and infestations	Urinary tract infection	3	Unrelated	Yes	04-Oct-2019	3	FALSE	08-Oct-2019	4
Infections and infestations	Lung infection	3	Unrelated	No	05-Oct-2019	4	FALSE		

Serious Adverse Events

There was one reported SAE during the AceticA trial.

Table 10. Line listing of the reported SAE

Randomisation Date	Onset Date	SAE Reason	Treatment	Other Causal Treatments	Event	Category	Grade	Other Events	CI Causality	PI Causality	SAE Categorisation	Outcome
01-Oct-2019	04-Oct-2019	Hospitalisation	Acetic Acid 2.0%	Urinary catherisation	Urinary tract infection	Infections and infestations	3	Infective exacerbation of COPD/chest sepsis from 05-Oct-2019 (Infections and infestations, Grade 3)	Unrelated	Unrelated	Unrelated SAE	Resolved - no sequelae

Conclusions

Acetic Acid was safe, well-tolerated and both concentrations led to a reduction in bacterial load. Use of 2.0% AA wound dressing showed a significant and sustained reduction in bacterial load when directly compared to 0.5% AA, warranting its use in future studies