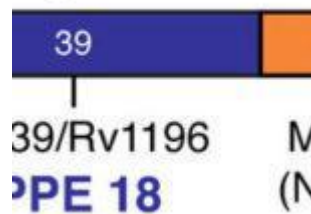
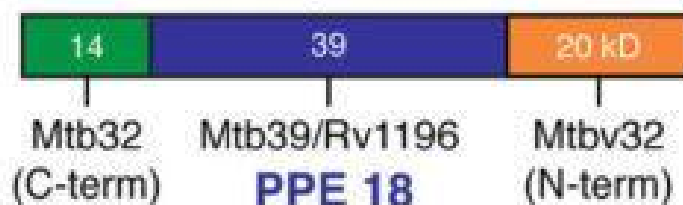


2018: The year of hope for TB vaccines

in protein in ASO



GSK M72 fusion protein in ASO-1E adjuvant



Schematic showing the position of PPE 18 (Mtb39a) in the M72 GSK vaccine. Source: [Brennan. Infection and Immunity 2017.](#)

The first ever [United Nations High Level meeting on Tuberculosis \(TB\) \(UNHLMTB\)](#) was held today (26th September). This meeting represents the acknowledgement and commitment of world leaders to strengthen action and investments towards the fight against TB.

Development of an efficacious vaccine that contributes to control of *Mycobacterium tuberculosis* (M.tb) infection and progression to TB disease has been identified as one of the tools required to achieve a *world without TB*. Currently, the only licenced tuberculosis vaccine BCG, confers limited efficacy against TB diseases in adolescents and adults. Highlighting the need for new improved TB vaccines that are protective post-adolescence.

On the eve of the UNHLMTB, results from the [Phase 2b M72/AS01E](#)

[vaccine trial were published in the NEJM](#). This study represents the first TB vaccine that is able to provide 54% protection against pulmonary tuberculosis diseases in individuals already infected with M.tb.

M72/AS01_E vaccine contains the recombinant M72 fusion protein of two M.tb antigens M.tb32A and M.tb39A combined with AS01_E adjuvant (the same adjuvant used in the malaria candidate vaccine RST,S AS01). Numerous phase 2(a) trial have been conducted (see Van Der Meeren et al., Supplementary Table S1 below). These studies have shown that M72/AS01_E is safe and highly immunogenic. Briefly, M72/AS01_E has been shown to induce polyfunctional Th1 CD4 T cells in both M.tb infected and uninfected HIV- individuals, as well as HIV+ individuals. Additionally, the vaccine has been shown to induce robust humoral responses.

Overall, the study published in NEJM represents a positive step forward in the fight against TB. It suggests that a vaccine that only has two M.tb antigens has the potential confer protection against pulmonary TB in M.tb infected individuals (in a TB endemic region).

**M.tb infection was based on positive QuantiFERON-TB Gold In Tube assay result, which measure immune reactivity to M.tb antigens CFP-10, ESAT-6 and TB7.7 antigens absent in BCG.*

Journal Article: Van Der Meeren et al., 2018. [Phase 2b Controlled Trial of M72/AS01_E Vaccine to Prevent Tuberculosis](#). The NEJM.

Also See: Bloom 2018. [New Promise for Vaccines against Tuberculosis](#). NEJM

Article by Cheleka AM Mpande

Journal Articles Listed in the Table Below.

Table B.1 Summary of available clinical data using WHO/OP or WHO

	Design	Country	Population	Age (years)	Schedule		Design	Time (h)	Outcome	Study conclusion
Levine et al. ¹	Phase III RCT	Belgium	140 subjects	5-65	2, 1 month		Study 01 (placebo), Study 02 (4000), Study 03 (8000), Study 04 (16000), Study 05 (32000)	140	Incidence of adverse events and response	0.01% mortality, decreased significantly higher adverse events for 16000. Trial resumed for the other treatments. Publication 1 (the response rates) follows?
Wattiaux et al. ²	Phase II RCT	the Netherlands	100 (10000)	5-65	2, 1 month		Study 01 (placebo), Study 02 (4000), Study 03 (8000), Study 04 (16000), Study 05 (32000), Study 06 (64000), Study 07 (128000)	100	Shortening time	0.005% mortality. Mortality of patients in hospitals that were significantly higher than 0.01% (0.02), Study 07 (0.01%), was selected for further development
David et al. ³	Phase II RCT	South Africa	100 (1000) and 100 (1000) + 1000	2-40	2, 1 month		Study 01 (placebo)	40	1, 10 and 100 mg daily, duration, investigation of 1- and 2-week	0.01% mortality. A statistically significant difference in mortality was observed between 1- and 2-week treatment. 1- and 2-week treatment was not superior to placebo
Wattiaux et al. ⁴	Phase III RCT	Belgium	100 (1000) (10000000)	5-65	2, 1 month		Study 01 (placebo), 0.01% were there	20	Response rate, adverse and 100 in 1000	0.01% mortality. No statistically significant difference in mortality between 1- and 2-week treatment
David et al. ⁵	Phase II RCT	South Africa	100 (1000) (10000000)	2-40	2, 1 month		Study 01 (placebo), 0.01%	20	Response rate, adverse and 100 in 1000	0.01% mortality. No statistically significant difference in mortality between 1- and 2-week treatment, suggesting the need for efficacy trial
David et al. ⁶	Phase II RCT	the Netherlands	100 (1000) (10000000)	2-40	2 and 1 month	Study 01 (placebo)	Study 01 (placebo), 0.01% were there Study 02 (4000), 0.01% were there Study 03 (8000), 0.01% were there Study 04 (16000), 0.01% were there Study 05 (32000), 0.01% were there Study 06 (64000), 0.01% were there Study 07 (128000), 0.01% were there Study 08 (256000), 0.01% were there Study 09 (512000), 0.01% were there Study 10 (1024000), 0.01% were there Study 11 (2048000), 0.01% were there Study 12 (4096000), 0.01% were there Study 13 (8192000), 0.01% were there Study 14 (16384000), 0.01% were there Study 15 (32768000), 0.01% were there Study 16 (65536000), 0.01% were there Study 17 (131072000), 0.01% were there Study 18 (262144000), 0.01% were there Study 19 (524288000), 0.01% were there Study 20 (1048576000), 0.01% were there Study 21 (2097152000), 0.01% were there Study 22 (4194304000), 0.01% were there Study 23 (8388608000), 0.01% were there Study 24 (16777216000), 0.01% were 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(1645504557321206042154969182557350504982735865633579863348609024000), 0.01% were there Study			

[illegible]

Adjusted System	Formulation	MP ₁ (°C)	MP ₂ (°C)	Flow Volume
APOL	30:70 water emulsion	35	35	1.0 mL
APOL	30:70 water emulsion	35	35	1.0 mL
APOL	30:70 water emulsion	35	35	1.0 mL
APOL	30:70 water emulsion	35	35	1.0 mL

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Table S1 Summary of available clinical data using Mtb72F or M72. Source Van Der Meeren et al., 2018 NEJM. Supplementary Material.