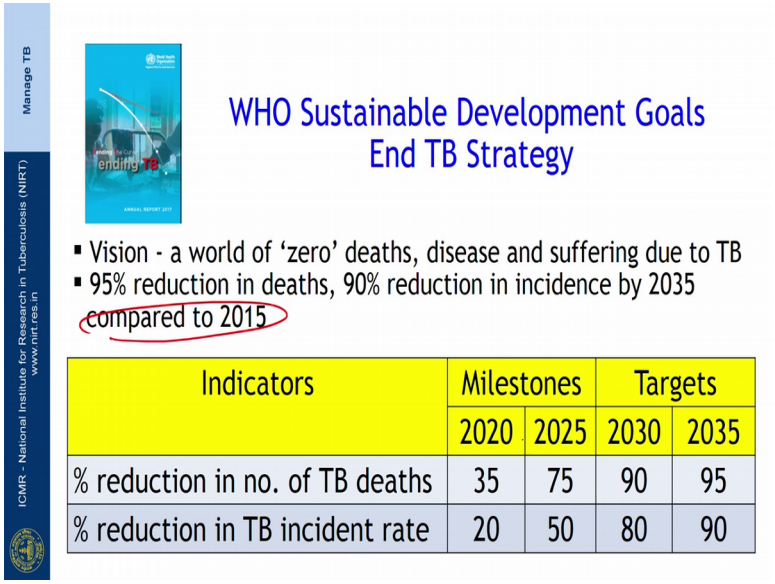
Manage TB
Dr. M S Jawahar
National Institute for Research in Tuberculosis, Chennai

Lecture - 61
Vaccine for TB Session 02

So, in this session on tuberculosis; Vaccine for Tuberculosis, we are going to look at what are the newer development as far as vaccines for TB is can is concerned.

(Refer Slide Time: 00:23)

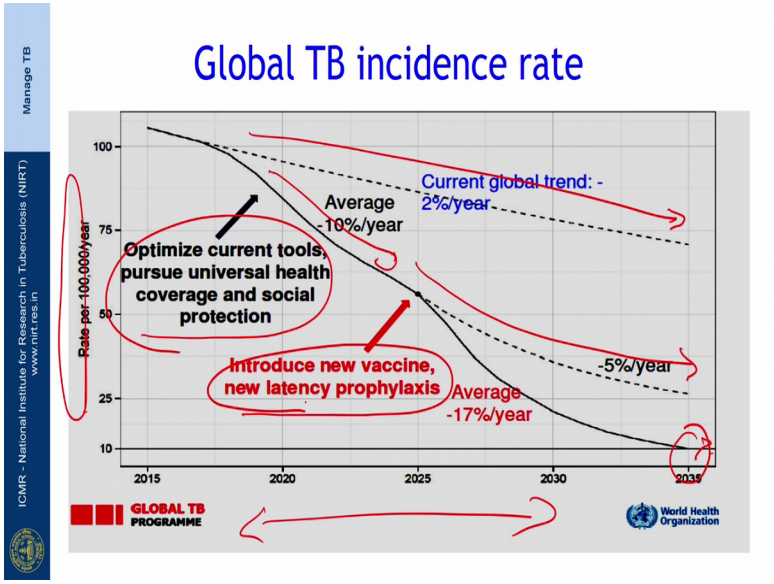


In the global efforts to control tuberculosis the WHO has enunciated certain strategies; we had the dot strategy in the 1990's followed by the stop TB strategy and currently we have the end TB strategy as part of the WHO sustainable development goals.

The end TB strategy envisages a world of 0 deaths disease and suffering due to TB and it aims at a 95 percent reduction in deaths, and 90 percent reduction in incidence of TB by the year 2035 compared to 2015. So, towards and then certain targets have been sent. So, if you want to achieve a percentage reduction in TB deaths of 95 percent by 2035 you need to reach targets of 35 75 and 90 over 2020, 2025, 2030.

Similarly, to reach a 90 percent reduction in TB deaths in TB incidence we need to have targets every 5 years. The Indian government has even a more ambitious strategy according the national strategic plan; we hope to achieve these targets by the year 2025 which is quite ambitious and therefore, special efforts are needed to achieve this target.

(Refer Slide Time: 02:00)

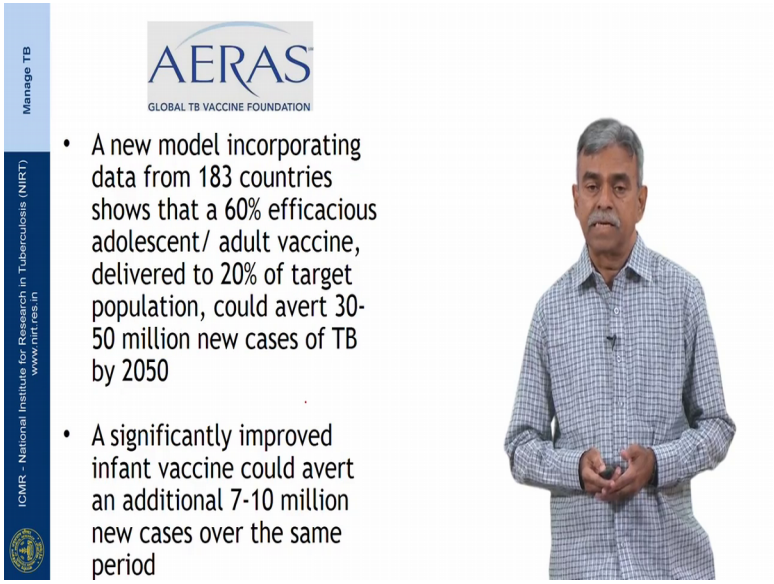


So, this slide shows you the global TB incidence rates the x axis shows the rate of TB the 100000 population per year, the y axis is the time 2015and two 2025.

The current rate of decline of TB incidence is about 2 percent per year. Now this rate of decline is not enough for us to achieve a 90 percent reduction in TB incidence rates which is this line. At the most we will receive achieve about 25 percent reduction by the year 2035. Now by optimizing the current tools that we have that diagnosis, more efficient treatment by seeing the numeral health coverage and social protection we can increase this decline to 10 percent per year and even then by the year 2035 you are not going to achieve a 90 percent reduction you may reach about 75 percent reduction.

Now, if you want to achieve the 90 percent reduction in incidence rates by 2035 you need to need introduced new vaccines and you need to treat latent TB only if these are done there is any hope of achieving these targets that have been set by the set as the end TB strategy of the WHO. Now the aeras is a nonprofit organization the global TB vaccine initiative and this organization is helping to facilitate the development of new TB vaccines that are affordable and available to the poorest sections of society.

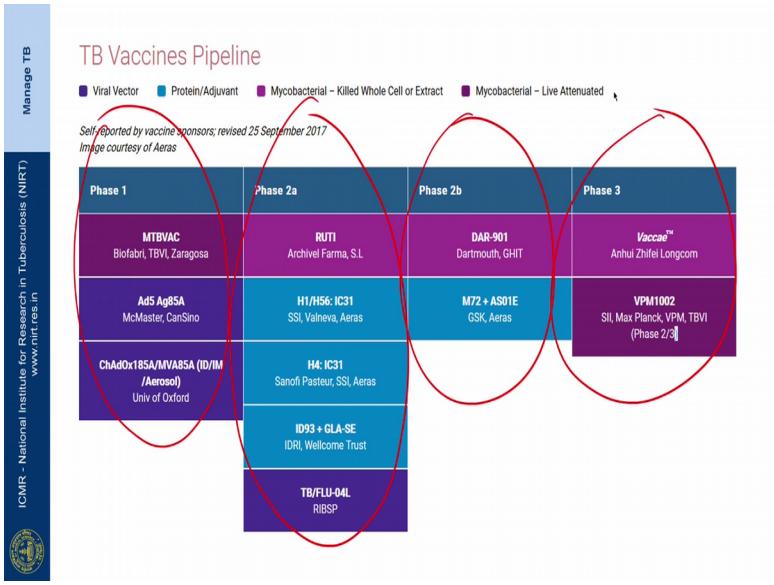
(Refer Slide Time: 03:54)



Aeras says that a new model incrop incorporating data from 183 countries shows that, a 60 percent efficacious adolescent or adult vaccine deliver to 20 percent of the target population could avert 30 to 50 million new TB cases by the year 2050.

And a significantly improved infant vaccine could avert an additional 7 to 10 million cases over the same period.

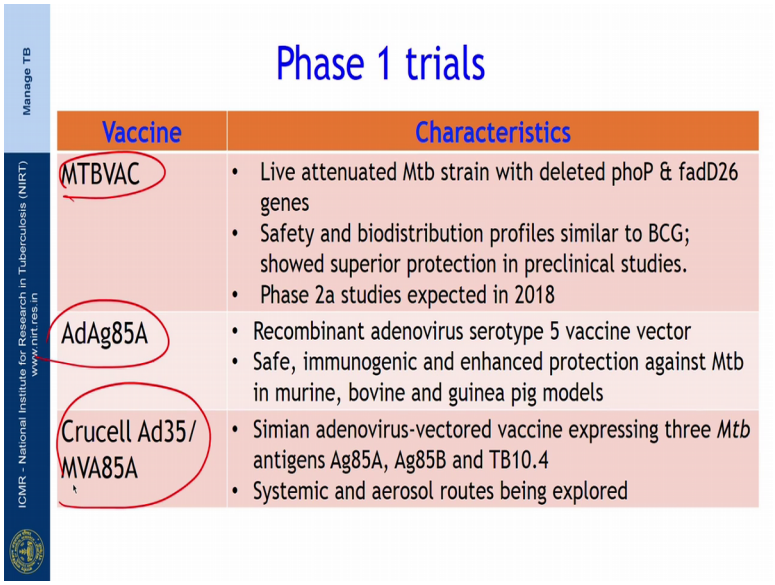
(Refer Slide Time: 04:21)



So, this slide tells you the TB vaccine pipeline, the global TB vaccine pipeline we see that there are 3 vaccines in phase 1, 5 vaccines in phase 2 a, 2 vaccines in phase 2 b and

2 vaccines in phase 3. I will briefly go through the characteristics of these vaccines in my next few slides.

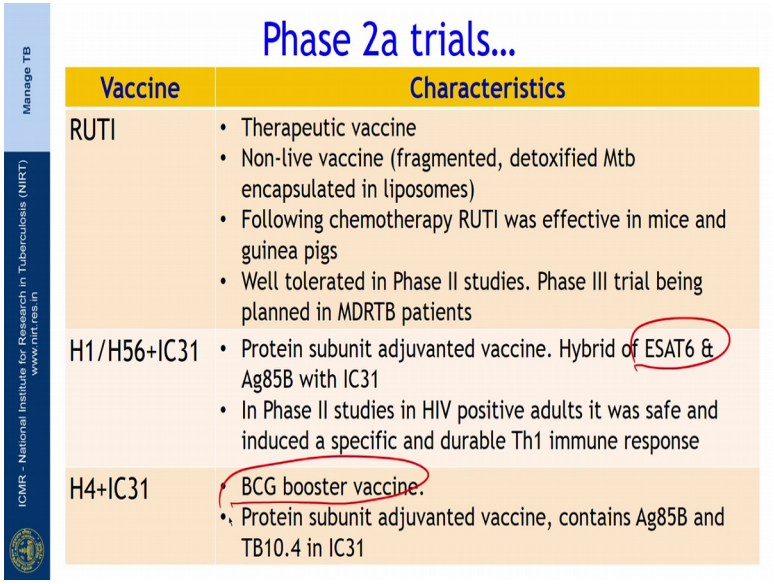
(Refer Slide Time: 04:45)



And in phase 1 we have 3 vaccines the MTBVAC these are live attenuated MTB strain with depleted phoP and fadD 26 genes, safety and by distribution profiles are similar to BCG and it shows superior protection in pinnacle studies; phase 2 a studies are expected in 2018.

The AdAg85A your recombinant adenovirus serotype 5 vaccine vector it is safe immunogenic and enhance protection against MTB in murine, bovine and guinea pig models. The Crucell AD85 the crucell 35 MVA 85 A is a simian adenovirus vectors vaccine expressing three MTB antigens antigen 85A, 85B and TB10.4 its being investigated in systemic and aerosol roots meaning that this is a vaccine that can be given by inhalation.

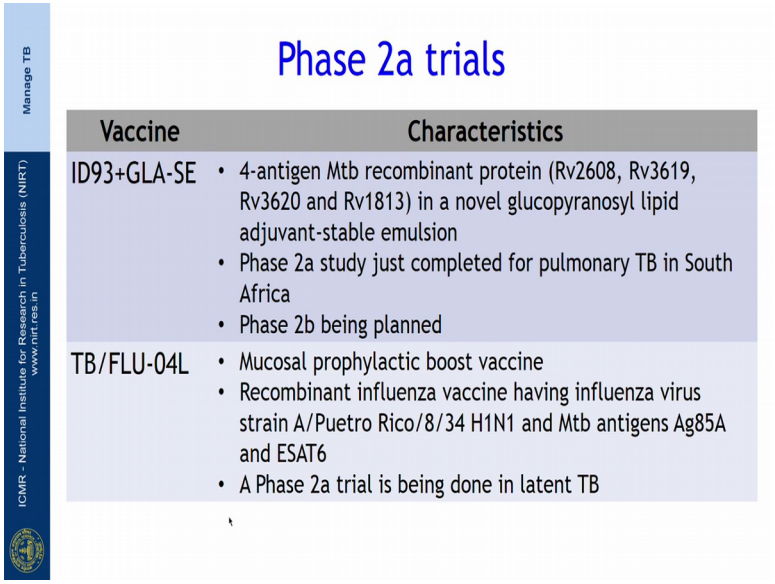
(Refer Slide Time: 05:52)



And the phase 2 a we have 5 vaccines the RUTI is a therapeutic vaccine it is a non live vaccine using fragmented detoxified MTB encapsulated in liposomes, following chemotherapy RUTI was effective in mice and guinea pigs its well tolerated in phase 2 studies, phase 3 trials are being planned in MDRTB patients the H 1 H 56, IC 31 and the HOIC 31 adjuvanted vaccines the H 1 H 56the protein subunit adjuvant or vaccine is a hybrid of ESAT 6 and antigen 85 B with adjuvant IC 31

In phase 2 studies in HIV positive adults it was safe and induced a specific and durable Th 1 immune response the H 4 IC 31 is a BCG booster vaccine and shows protection protein subunit adjuvanted vaccine contains AG 85 B and TB 10.4 in IC 31.

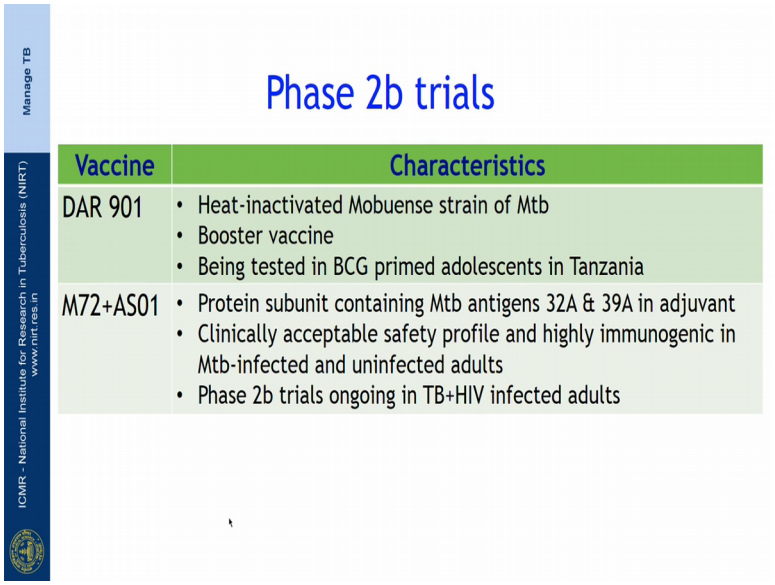
(Refer Slide Time: 07:03)



The ID 93 GLA-SE is a 4 antigen MTB recombinant protein containing Rv 2608, 3619, 3620 and 1813 in a novel glucopyranosyl lipid adjuvant stable emulsion.

Phase 2 a study just completed for pulmonary TB in South Africa and phase 2 b study is being planned the TB FLU-04 L is a mucosal prophylactic boost vaccine again can be given by a narration; it is the recombinant influenza vaccine having influenza virus strains H 1 N 1 and MTB antigen 85 A and ESAT 6 a phase 2 a trial is being done in latent TB.

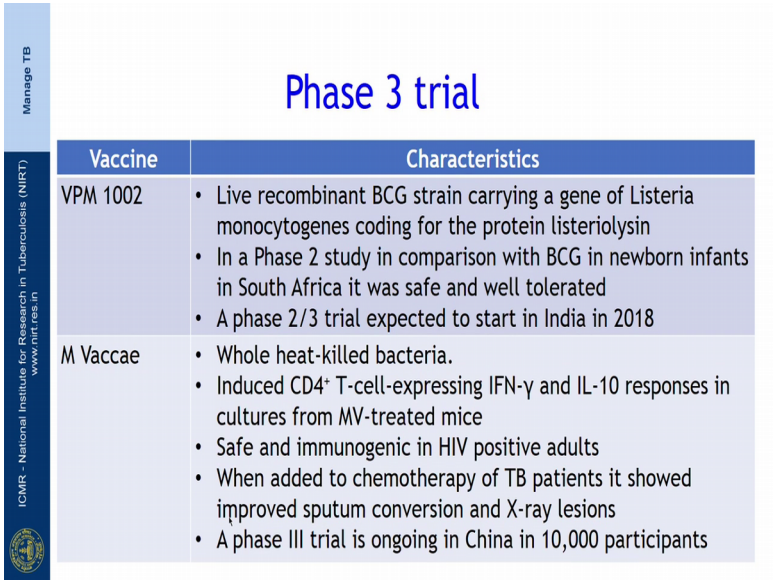
(Refer Slide Time: 07:52)



And the phase 2 b we have 2 vaccines the DAR 901, which is a heat inactivated mobuense strain of MTB its again a booster vaccine is being tested in BCG primed adolescents in tanzania and the M 72 AS 01 vaccine which is a protein subunit containing MTB antigens 32 A and 39 A in adjuvant.

Clinically accepted safety profile has been shown and highly immunogenic in MTB infected uninfected adults phase 2 b trials are ongoing in HIV, TB infected adults.

(Refer Slide Time: 08:31)

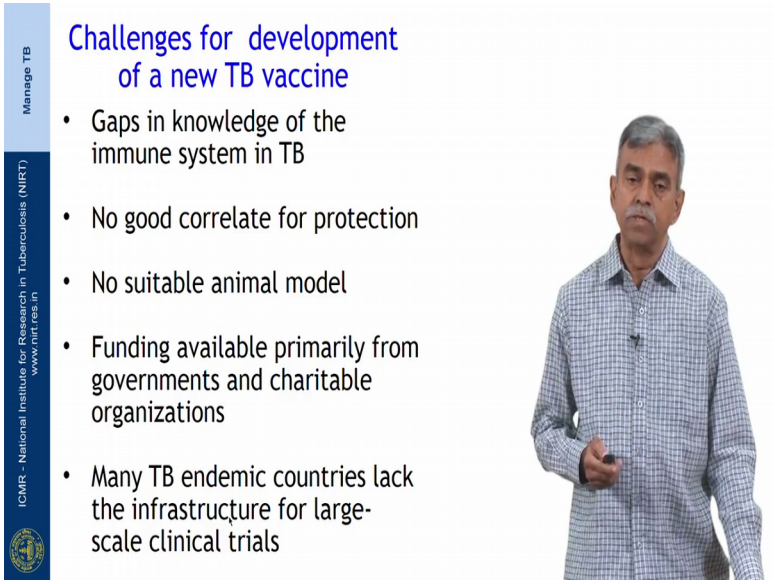


And in phase 3 which is the most advanced stages of clinical trials we have 2 vaccines the VPM 1002; it is a live recombinant BCG strain carrying a gene for listeria monocytogenes, coding for the protein the serialization.

In phase 2 studies in comparison BCG in newborn infants in South Africa it was shown to be safe and well tolerated and a phase 2 3 trial is expected to start in India in 2018 and M Vaccae is a whole heat-kill bacteria vaccine induces CD 4 T-cell expressing interferon gamma and iolite responses in cultures from MV treated mice is safe an immunogenic in HIV positive adults when added to chemotherapy of TB patients it should improve sputum conversion and X-ray lesions.

So, it is a therapeutic vaccine and a phase 2 trial is ongoing in China with more than 10000 participants.

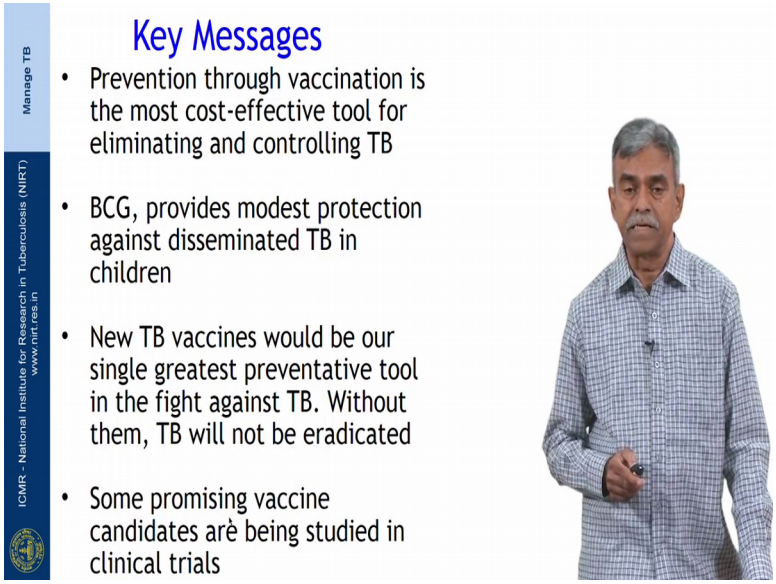
(Refer Slide Time: 09:32)



So, what are the challenges for developing of new TB vaccine? There are gaps in our knowledge from the immune response system in TB there is no good correlate for protection, we do not know what really constitutes protection and tuberculosis, there is no suitable animal model, funding is difficult only governments and charitable organizations are willing to fund for TB vaccines because there is no market for a TB drug or vaccine.

Industry is reluctant to fund TB vaccines and many TB endemic countries like the infrastructure to carry out large clinical trials that are necessary to or test out TB vaccines.

(Refer Slide Time: 10:16)



So, the key messages in my lecture today that the prevention through vaccination is a most cost effective tool for eliminating and controlling tuberculosis. BCG provides only modest protection against disseminated TB in children. New TB vaccines would be our single greatest preventative tool in the fight against tuberculosis; without them there is no hope that TB will be eradicated. And some promising vaccine candidates are being studied in clinical trials.

Thank you.