

Table 1. Studies on effects of immune therapy in patients with drug-sensitive tuberculosis

First author	Year	Agent	Design	No. of patients	Dose	Delivery	Duration of treatment	Response to treatment
Giosue S	1998	IFN-	Prospective controlled	10 vs. 10	300 *MU, 3 /weeks	Inhalation	2 months	Rapid bacteriologic and radiographic improvement in IFN- group
Stanford JL	1990	Killed <i>M. vaccae</i>	Prospective controlled	47 vs. 65	10 ⁹	ID injection	One injection	No difference in bacteriologic and radiographic improvement
Onyebujoh PC	1995	Killed <i>M. vaccae</i>	Prospective controlled	180	10mg	ID injection	One injection	Rapid bacteriologic response Low mortality (0% vs. 40%)
Durban Immunotherapy Trial Group	1999	Killed <i>M. vaccae</i>	Prospective controlled	172 vs. 175	10 ⁹	ID injection	One injection	No difference in culture conversion rate and in the time to a negative culture
Johnson JL	2000	Killed <i>M. vaccae</i>	Prospective controlled	61 vs. 59	10 ⁹	ID injection	One injection	Rapid bacteriologic response Bigger improvement in radiographs
Mwinga A	2002	Killed <i>M. vaccae</i>	Prospective controlled	109 vs. 107	10 ⁹	ID injection	One injection	No difference in bacteriologic response and mortality
Wang W	1999	Killed <i>M. vaccae</i>	Prospective controlled	35 vs. 35	-	-	-	Rapid bacteriologic response
Luo Y	2001	Killed <i>M. vaccae</i>	Prospective controlled	171 vs. 171	-	-	-	Rapid bacteriologic and radiographic response

Abbreviations: *MU = Million Unit, ID = Intradermal

2. Interferon-

oxide, nitric oxide , MHC Fc
 가 , pH ,
 16,17 .
 , NK cell , interferon-
 presentation), 가 , (Antigen
 Th1 , Th2 8 ,
 Th1 9 .
 interferon- CD4+ T 가
 IL-4 10 .
 Interferon- 가 ,
 Giosue S , 20
 HIV ,
 isoniazid, rifampicin, pyrazinamide, etha-
 mbutol
 2 3 (aerosolized) interferon-
 (300 Unit) 11 .
 interferon- 가
 가 ,
 . 1999 Pa-
 lmero 5 4 R 4
 1 Interferon-2 b 300 Unit ,
 2 5 3
 12 . 2000 interferon- 6
 가 7
 가 13 , 3
 interferon- (300 Unit) 2
 5
 , interferon-

Interferon- 가
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 19
 interferon-
 , 가 20 .
 Interferon-
 1997 Condos 21 . 5
 500µg interferon-
 3 1
 . 5
 가 가 ,
 . 2004 Suarez - Mendez
 8
 100 IU
 5 3
 ,
 22 .
 interferon-
 . 6
 interferon- 3 200 IU 6

3. Interferon-

Interferon-
 IL-12 IL-18
 가 14,15 . Interferon-
 super-

23 .
 interferon-
 6 200 IU interferon-
 4 7 3 , 6
 2 interferon-
 24 . 8 200 IU
 interferon- 3.5 7 3
 25 .

Table 2. Studies on effects of immune therapy in patients with multi-drug resistant tuberculosis

First author	Year	Agent	Design	No. of patients	Dose	Delivery	Duration of treatment	Response to treatment
Johnson B	1995	IL-2	One-arm	7	12.5µg, 2/day	*IM injection	30 days	Smear conversion: 5/7 Culture conversion: 0/7
Johnson B	1997	IL-2	Prospective controlled (Daily vs. Pulse vs. Placebo)	12 vs. 9 vs.12	12.5µg, 2/day	IM injection	30 days	Culture conversion: 5/8 vs. 2/7 vs. 2/8
Palmero D	1999	IFN- 2b	One-arm	5	300 IU, 1/week	¹ SC injection	4 months	Culture conversion; 2/5
Giosue S	2000	IFN-	One-arm	7	300 IU, 3 /weeks	Inhalation	2 months	Transient smear conversion: 5/7 Culture conversion: 0/7
Condos R	1997	IFN-	One-arm	5	500µg, 3/week	Inhalation	1 month	Smear conversion: 5/5 Culture conversion: 0/5
Suarez- Mendez R	2004	IFN-	One-arm	8 (MDR-TB; 4)	100IU, 1/day for 1 mo 3/week for 5 mos	IM injection	6 months	Culture conversion: 8/8
Koh WJ	2004	IFN-	One-arm	6	200M IU, 3/weeks	Inhalation	6 months	Radiographic improvement: 5/6 Culture conversion: 0/6
Kim EK	2004	IFN-	One-arm	6	200M IU, 3/weeks	SC injection	4-7 months	Transient culture conversion: 2/6
Park SK	2004	IFN-	One-arm	8	200M IU, 3/weeks	SC injection	3.5-7 months	Culture conversion: 0/8
Luo Y	2000	Killed <i>M. vaccae</i>	Prospective controlled	28 vs. 28	-	-	-	More culture conversion at 6 months of treatment

Abbreviations: *IM = Intramuscular, ¹SC = Subcutaneous

interferon-가
interferon-
4. *Mycobacterium vaccae*
Mycobacterium vaccae 가
mycobacteria
Th2
26
Mycobacterium vaccae
1990
1990 Stanford 47
1 *Mycobacterium*
vaccae 65
, *Mycobacterium vaccae*
가 가
가 27
My-
cobacterium vaccae 1,2,3
, 28
Mycobacterium vaccae
. 1999 Durban Immun-
otherapy Trial Group 347
(HIV) *Mycobacterium vaccae*
가
가 29
2002 Mwinga
A HIV *Mycobacterium*
vaccae 가 가
, 109 *Mycobacterium vaccae*
107
30
, 2000 HIV
120

Mycobacterium vaccae
31
Mycobacterium vaccae
Mycobacterium vaccae
32,33
6
34
Mycobacterium vaccae
interferon-
cytokine *Mycobacterium vaccae*
가
가
cytokine 가가
oxazolidinone linezolid

1. WHO. Stop TB: 2001 annual report. 2002.
2. Dye C, Espinal MA, Watt CJ, Mbiaga C, Williams BG. Worldwide incidence of multidrug-resistant tuberculosis. *J Infect Dis* 2002;185:1197-202.
3. Mukherjee JS, Rich ML, Socci AR, Joseph JK, Viru

- FA, Shin SS, et al. *Programmes and principles in treatment of multidrug-resistant tuberculosis. Lancet* 2004;363:474-81.
- Smith KA. *Interleukin-2: inception, impact, and implications. Science* 1988;240:1169-76.
 - Kuziel WA, Greene WC. *Interleukin-2 and the IL-2 receptor: new insights into structure and function. J Invest Dermatol* 1990;94:27S-32S.
 - Johnson BJ, Ress SR, Willcox P, Pati BP, Lorgat F, Stead P, et al. *Clinical and immune responses of tuberculosis patients treated with low-dose IL-2 and multidrug therapy. Cytokines Mol Ther* 1995;1:185-96.
 - Johnson BJ, Bekker LG, Rickman R, Brown S, Lesser M, Ress S, et al. *rhIL-2 adjunctive therapy in multidrug resistant tuberculosis: a comparison of two treatment regimens and placebo. Tuber Lung Dis* 1997;78:195-203.
 - Belardelli F. *Role of interferons and other cytokines in the regulation of the immune response. APMIS* 1995;103:161-79.
 - Romagnani S. *Induction of TH1 and TH2 responses: a key role for the 'natural' immune response? Immunol Today* 1992;13:379-81.
 - Brinkmann V, Geiger T, Alkan S, Heusser CH. *Interferon alpha increases the frequency of interferon gamma-producing human CD4+ T cells. J Exp Med* 1993;178:1655-63.
 - Giosue S, Casarini M, Alemanno L, Galluccio G, Mattia P, Pedicelli G, et al. *Effects of aerosolized interferon-alpha in patients with pulmonary tuberculosis. Am J Respir Crit Care Med* 1998;158:1156-62.
 - Palmero D, Eiguchi K, Rendo P, Castro Zorrilla L, Abbate E, Gonzalez Montaner LJ. *Phase II trial of recombinant interferon-alpha2b in patients with advanced intractable multidrug-resistant pulmonary tuberculosis: long-term follow-up. Int J Tuberc Lung Dis* 1999;3:214-8.
 - Giosue S, Casarini M, Ameglio F, Zangrilli P, Palla M, Altieri AM, et al. *Aerosolized interferon-alpha treatment in patients with multi-drug-resistant pulmonary tuberculosis. Eur Cytokine Netw* 2000;11:99-104.
 - Tomura M, Maruo S, Mu J, Zhou XY, Ahn HJ, Hamaoka T, et al. *Differential capacities of CD4+, CD8+, and CD4-CD8- T cell subsets to express IL-18 receptor and produce IFN-gamma in response to IL-18. J Immunol* 1998;160:3759-65.
 - Mountford AP, Coulson PS, Cheever AW, Sher A, Wilson RA, Wynn TA. *Interleukin-12 can directly induce T-helper 1 responses in interferon-gamma (IFN-gamma) receptor-deficient mice, but requires IFN-gamma signalling to downregulate T-helper 2 responses. Immunology* 1999;97:588-94.
 - Murray HW. *Current and future clinical applications of interferon-gamma in host antimicrobial defense. Intensive Care Med* 1996;22(Suppl 4):S456-61.
 - Darnell JE Jr. *Studies of IFN-induced transcriptional activation uncover the Jak-Stat pathway. J Interferon Cytokine Res* 1998;18:549-54.
 - Flynn JL, Chan J, Triebold KJ, Dalton DK, Stewart TA, Bloom BR. *An essential role for interferon gamma in resistance to Mycobacterium tuberculosis infection. J Exp Med* 1993;178:2249-54.
 - Dorman SE, Holland SM. *Mutation in the signal-transducing chain of the interferon-gamma receptor and susceptibility to mycobacterial infection. J Clin Invest* 1998;101:2364-9.
 - Holland SM, Eisenstein EM, Kuhns DB, Turner ML, Fleisher TA, Strober W, et al. *Treatment of refractory disseminated nontuberculous mycobacterial infection with interferon gamma: a preliminary report. N Engl J Med* 1994;330:1348-55.
 - Condos R, Rom WN, Schluger NW. *Treatment of multidrug-resistant pulmonary tuberculosis with interferon-gamma via aerosol. Lancet* 1997;349:1513-5.
 - Suarez-Mendez R, Garcia-Garcia I, Fernandez-Olivera N, Valdes-Quintana M, Milanes-Mirelles MT, Carbonell D, et al. *Adjuvant interferon gamma in patients with drug-resistant pulmonary tuberculosis: a pilot study. BMC Infect Dis* 2004;4:44.
 - Koh WJ, Kwon OJ, Suh GY, Chung MP, Kim H, Lee NY, et al. *Six-month therapy with aerosolized interferon-gamma for refractory multidrug-resistant pulmonary tuberculosis. J Korean Med Sci* 2004;19:167-71.
 - Kim EK, Shim TS, Lee JY, Oh YM, Lim CM, Lee SD, et al. *The adjuvant effect of subcutaneous interferon-gamma in the treatment of refractory multidrug-resistant pulmonary tuberculosis. Tuberc Respir Dis* 2004;57:226-33.
 - Park SK, Chen DS, Lee IH, Lee DH. *Treatment of multidrug-resistant pulmonary tuberculosis with interferon-gamma subcutaneous injection. Tuber Lung Dis* 2004;55:S99.
 - Stanford JL, Rook GA, Bahr GM, Dowlati Y, Ganapati R, Ghazi Saidi K, et al. *Mycobacterium vaccae in immunoprophylaxis and immunotherapy of leprosy and tuberculosis. Vaccine* 1990;8:525-30.
 - Stanford JL, Bahr GM, Rook GA, Shaaban MA, Chugh TD, Gabriel M, et al. *Immunotherapy with Mycobacterium vaccae as an adjunct to chemotherapy in the treatment of pulmonary tuberculosis. Tubercle*

- 1990;71:87-93.
28. Onyebujoh PC, Abdulmumini T, Robinson S, Rook GA, Stanford JL. *Immunotherapy with Mycobacterium vaccae as an addition to chemotherapy for the treatment of pulmonary tuberculosis under difficult conditions in Africa. Respir Med 1995;89:199-207.*
 29. Durban Immunotherapy Trial Group. *Immunotherapy with Mycobacterium vaccae in patients with newly diagnosed pulmonary tuberculosis: a randomised controlled trial. Lancet 1999;354:116-9.*
 30. Mwinga A, Nunn A, Ngwira B, Chintu C, Warndorff D, Fine P, et al. *Mycobacterium vaccae (SRL172) immunotherapy as an adjunct to standard anti-tuberculosis treatment in HIV-infected adults with pulmonary tuberculosis: a randomised placebo-controlled trial. Lancet 2002;360:1050-5.*
 31. Johnson JL, Kanya RM, Okwera A, Loughlin AM, Nyole S, Hom DL, et al. *Randomized controlled trial of Mycobacterium vaccae immunotherapy in non-human immunodeficiency virus-infected ugandan adults with newly diagnosed pulmonary tuberculosis. J Infect Dis 2000;181:1304-12.*
 32. Wang W, Jin G, Ye Y, Xia X, Wang A, Zhuang Y, et al. *A clinical study on vaccine of Mycobacterium vaccae in treating pulmonary tuberculosis. Zhonghua Jie He He Hu Xi Za Zhi 1999;22:108-10.*
 33. Luo Y. *The immunotherapeutic effect of Mycobacterium vaccae vaccine on initially treated pulmonary tuberculosis. Zhonghua Jie He He Hu Xi Za Zhi 2001;24:43-7.*
 34. Luo Y, Lu S, Guo S. *Immunotherapeutic effect of Mycobacterium vaccae on multi-drug resistant pulmonary tuberculosis. Zhonghua Jie He He Hu Xi Za Zhi 2000;23:85-8.*
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