



Miltenyi Biotec

Reference list

CliniMACS® CD25 System

CD25 Enrichment

General

Reviews

Minimum information about T Regulatory Cells: a step toward Reproducibility and standardization.

Fuchs, A. et al

Frontiers in Immunology (2018)8: 1844

T regulatory cell separation for clinical application.

Di Ianni M, Del Papa B, Zei T, Iacucci Ostini R, Cecchini D, Cantelmi MG, Baldoni S, Sportoletti P, Cavalli L, Carotti A, Pierini A, Falini B, Martelli MF, Falzetti F.

Transfus Apher Sci. (2012) Oct;47(2):213-6.

Clinical perspectives for regulatory T cells in transplantation tolerance.

Hippen, K.L., Riley, J.L., June, C.H., Blazar, B.R.

Semin. Immunol. (2011) 23 (6):462-8.

Treg cells: Collection, processing, storage and clinical use.

Daniele, N., Scerpa, M.C., Landi, F., Cniglia, M., Miele, M.J., Locatelli, F., Isacchi, G., Zinno, F.

Pathology- Research and Practice (2011) 207:209-215.

Haploidentical hematopoietic transplantation: current status and future perspectives.

Reisner, Y., Hagin, D. and Martelli, M.F.

Blood (2011) Dec.1; 118(23):6006-17.

Performance / Expansion data

A Rapamycin-based GMP Compatible Process for the Isolation and Expansion of Regulatory T cells for Clinical Trials

Fraser H., Safinia N., Grageda N., Thirkell S., Lowe K., Fry L., Scotta C., Hope A., Fisher C., Hilton R., Game D., Harden P., Bushell A., Wood K., Lechler R.I., Lombardi G. Molecular Therapy Methods and Clinical Development (2018)

Good Manufacturing Practice-Compliant Production and Lot-Release of Ex Vivo Expanded Regulatory T Cells As Basis for Treatment of Patients with Autoimmune and Inflammatory Disorders.

Wiesinger M., Stoica D., Roessner S., Lorenz C., Fischer A., Atreya R., Neufert C. F., Atreya I., Scheffold A., Schuler-Thurner B., Neurath M. F., Schuler G. and Voskens C. J.

Front. Immunol. (2017) 8:1371. doi:

10.3389/fimmu.2017.01371

Characterization and Expansion of Autologous GMP-ready Regulatory T Cells for TREG-based Cell Therapy in Patients with Ulcerative Colitis.

Voskens C.J., Fischer A., Roessner S., Lorenz C., Hirschmann S., Atreya R., Neufert C., Atreya I., Neurath M., Schuler G.

Inflamm Bowel Dis (2017) 23:1348–1359

Clinical-grade regulatory T cells: Comparative analysis of large-scale expansion conditions.

Velaga, S., Alter, C., Dringenberg, U., Thiesler, C.T., Kuhs, S., Olek, S., Ukena, S.N., Franzke, A.

Experimental Hematology (2016) Sep 27. pii: S0301-472X(16)30620-8

A robust, good manufacturing practice-compliant, clinical-scale procedure to generate regulatory T cells from patients with amyotrophic lateral sclerosis for adoptive cell therapy.

Alsuliman, A., Appel, S.H., Beers, D.R., Basar, R., Shaim, H., Kaur, I., Zulovich, J., Yvon, E., Muftuoglu, M., Imahashi, N., Kondo, K., Liu, E., Shpall, E.J., Rezvani, K. Cytotherapy. (2016) Oct;18(10):1312-24

Successful expansion of functional and stable regulatory T cells for immunotherapy in liver transplantation.

Safinia N, Vaikunthanathan T, Fraser H, Thirkell S, Lowe K, Blackmore L, Whitehouse G, Martinez-Llordella M, Jassem W, Sanchez-Fueyo A, Lechler RI, Lombardi G. *Oncotarget*. (2016) Jan 17.

GMP validation of large-scale expansion of regulatory T cells from patients affected by liver and kidney failure.

C. Lavazza, M. Viganò, T. Montemurro, E. Montelatici, S. Budelli, M. G. Cannone, S. Savelli, F. Ulbar, L. Catani, V. Giudice, M. Cescon, G. La Manna, R. M. Lemoli, R. Giordano.

ISCT Meeting (2017) poster presentation

An innovative method to generate a Good Manufacturing Practice-ready regulatory T-cell product from non-mobilized leukapheresis donors.

Zhang W., Smythe J, Frith E, Belfield H, Clarke S, Watt SM, Danby R, Benjamin S, Peniket A, Roberts DJ. *Cytotherapy*, (2015) Sep;17(9):1268-79.

Clinical-grade separation and expansion of regulatory T cells for clinical studies on cell therapy in solid organ transplantation.

Fazekasova H., Thirkell, S. Lowe K., Bushell A., and Lombardi G., *MACS&more Vol 15 – 2/2013*

Regulatory T cells (Tregs) GMP production for clinical application: phenotypic and functional analysis of cryopreserved/thawed healthy Tregs.

Ulbar, F., Viganò M., Sinigallia B.; Dan E., Montemurro T., Lavazza C., Chirumbolo G., Sciulli E., Giudice V., Bonifazi F., Bandini, G., Giordano R., Cavo M., Catani L., Arpinati M. *EBMT (2017) poster presentation*

Purification and Expansion of Antigen-Specific Human Tregs for Clinical Application Using a Single Step CD25 Positive Selection.

Beato F., Veerapathran A., Pidala J., Janssen W.E., Anasetti C.

ASH Meeting (2012), poster presentation

Clinical scale enrichment and expansion of highly pure CD25+FoxP3 regulatory T cells.

Conrads, C., Schmitz, J., Assenmacher, M., Niemand, C., Scheffold, A. *ASH Meeting, (2010), Poster abstract 3718.*

Clinical Grade Treg: GMP Isolation, Improvement of Purity by CD127pos Depletion, Treg Expansion, and Treg Cryopreservation.

Peters, J.H., Preijers, F.W., Woestenenk, R., Hilbrands, L.B., Koenen, H.J., and Joosten, I.

PLoS ONE (2008) Sept. 21; 3(9): e3161.

Clinical-grade preparation of human natural regulatory T cells encoding the thymidine kinase suicide gene as a safety gene.

Guillot-Delost, M., Cherai, M., Hamel, Y., Rosenzweig, M., Baillou, M., Simonin, G., Leclercq, V., Mariotti-Ferrandiz, M.E., Six, A., Bon-Durand, V., Maury, S., Salomon, B.L., Cohen, J.L., Klatzmann, D., and Lemoine, F.M.

J. Gene Med (2008) Aug; 10(8): 834-46.

Isolation of CD4+CD25+ Regulatory T Cells for Clinical Trials.

Hoffmann, P., Boeld, T.J., Eder, R., Albrecht, J., Doser, K., Piseshka, B., Dada, A., Niemand, C., Assenmacher, M., Orsó, E., Andreesen, R., Holler, E., and Edinger, M. *ASBMT (2006) 12(3): 243-37.*

Large Scale In Vitro Expansion of Polyclonal Human CD4+CD25high Regulatory T Cells.

Hoffmann, P., Eder, R., Kunz-Schughart, L.A., Andreesen, R., and Edinger, M.

Blood (2004) Aug 1; 104(3): 895-903.

Hematopoietic stem cell transplantation

Treg-protected donor lymphocyte infusions: a new tool to address the graft-versus-leukemia effect in the absence of graft-versus-host disease in patients relapsed after HSCT.

Di Ianni M., Oliosio P., Giancola R., Santarone S., Natale A., Papalinetti G., Villanova I., Baldoni S., Di Tommaso A., Bonfini T., Accorsi P., Di Bartolomeo P. *Int J Hematology (2017) https://doi.org/10.1007/s12185-017-2292-3*

Clinical-Grade–Expanded Regulatory T Cells Prevent Graft-versus-Host Disease While Allowing a Powerful T Cell–Dependent Graft-versus-Leukemia Effect in Murine Models.

Del Papa B., Ruggeri L., Urbani E., Baldoni S., Cecchini D., Zei T., Iacucci Ostini R., Crescenzi B., Carotti A., Pierini A., Sportoletti P., Di Bartolomeo P., Falzetti F., Mecucci C., Velardi A., Martelli M. F., Di Ianni M. *Biol. Blood Marrow Transpl. (2017) July, in press*

Infusion of clinical-grade enriched regulatory T cells delays experimental xenogeneic graft-versus-host disease.

Hannon M, Lechanteur C, Lucas S, Somja J, Seidel L, Belle L, Bruck F, Baudoux E, Giet O, Chantillon AM, Delvenne P, Drion P, Beguin Y, Humblet-Baron S, Baron F. *Transfusion. (2014) Feb;54(2):353-63.*

Robust and cost effective expansion of human regulatory T cells highly functional in a xenograft model of graft-versus-host disease.

Chakraborty R, Mahendravada A, Perna SK, Rooney CM, Heslop HE, Vera JF, Savoldo B, Dotti G. *Haematologica. (2013) Apr; 98(4):533-7.*

T regulatory cell separation for clinical application

Di Ianni M, Del Papa B, Zei T, Iacucci Ostini R, Cecchini D, Cantelmi MG, Baldoni S, Sportoletti P, Cavalli L, Carotti A, Pierini A, Falini B, Martelli MF, Falzetti F.

Transfus Apher Sci. (2012) Oct;47(2):213-6.

Commentary: CD4+ CD25+ approach in the clinic.

Edinger M.

Cytotherapy (2008) 10(7): 655-656.

Immunomagnetic isolation of CD4+CD25+FoxP3+ natural T regulatory lymphocytes for clinical applications.

Di Ianni, M., Del Papa, B., Cecchini, D., Bonifacio, E., Moretti, L., Zei, T., Iacucci Ostini, R., Falzetti, F., Fontana, L., Tagliapietra, G., Maldini, C., Martelli M.F., and Tabilio, A. Clin. Exp. Immunol. (2009) 156: 246–253.

Next generation HLA-haploidentical HSCT

Martelli MF, Ianni MD, Ruggeri L., Falzetti F., Carotti A., Reisner Y., and Velardi A. Bone Marrow Transplantation (2015) 50, 63–66

Adoptive transfer of allogeneic regulatory T cells into patients with chronic graft-versus-host disease.

Theil A, Tuve S, Oelschlägel U, Maiwald A, Döhler D, Oßmann D, Zenkel A, Wilhelm C, Middeke JM, Shayegi N, Trautmann-Grill K, von Bonin M, Platzbecker U, Ehninger G, Bonifacio E, Bornhäuser M.

Cytotherapy. (2015) Apr;17(4):473-86.

HLA-haploidentical transplantation with regulatory and conventional T-cell adoptive immunotherapy prevents acute leukemia relapse

Martelli MF, Di Ianni M, Ruggeri L, Falzetti F, Carotti A, Terenzi A, Pierini A, Massei MS, Amico L, Urbani E, Del Papa B, Zei T, Iacucci Ostini R, Cecchini D, Tognellini R, Reisner Y, Aversa F, Falini B, Velardi A. Blood. (2014) Jul 24;124(4):638-44.

Chemotherapy-Based HLA Haploidentical Transplantation with Treg/Tcon Immunotherapy in Unfit/Elderly Leukemia Patients

Carotti A., Ruggeri L., Falzetti F., Di Ianni M., Terenzi A., Amico L., Pierini A., Speranza Massei M., Piccinelli S., Ciardelli S., Zei T., Iacucci R., Felicini R., Martelli M.F., Velardi A. EBMT (2017) poster presentation

Adoptive immunotherapy with Tregs and Tcons rebuilds post transplant immunity and is associated with low TRM in HLA-haploidentical transplantation

M. Di Ianni, F. Falzetti, A. Carotti, A. Terenzi, A. Pierini, M. Speranza Massei, L. Ruggeri, A. Velardi, M.F. Martelli EBMT Meeting (2013), oral presentation O143

Adoptive immunotherapy with Tregs and Tcons promote a GvL effect in absence of GvHD in HLA-haploidentical transplantation

M. Di Ianni, F. Falzetti, A. Carotti, A. Terenzi, A. Pierini, M.S. Massei, A. Velardi, F. Aversa, M.F. Martelli EBMT Meeting (2011) oral presentation (O154)

Adoptive Immunotherapy with Tregs and Tcons ensures low TRM and a low incidence of post-transplant leukaemia relapse after HLA haploidentical transplants for acute leukemia.

Di Ianni, M., Falzetti, F., Carotti, A., Terenzi, A., Ruggeri, L., Antonio, P., de Vazio, V., Zoi, V., Massei, M.S., Reisner, Y., Velardi, A., Aversa, F., and Martelli, M.F. ASH Meeting (2011), Oral abstract 154.

Donor-type CD4+CD25+ regulatory T cells in HLA-matched allogeneic SCT.

Edinger M.

ASH Meeting (2008), Miltenyi Biotec Corporate Symposia

Immunoselection and clinical use of T regulatory cells in HLA-haploidentical stem cell transplantation.

Di Ianni, M., Falzetti, F., Carotti, A., Terenzi, A., Del Pap, B., Perruccio, K., Ruggeri, L., Sportoletti, P., Rosati, E., Marconi, P., Falini, B., Reisner, Y., Verlardi, A., Aversa, F., and Martelli, M.F.

Best Practice & Research Clinical Haematology (2011) 24: 459-466.

Tregs prevent GvHD and promote immune reconstitution in HLA-haploidentical transplantation.

Di Ianni, M., Falzetti, F., Carotti, A., Terenzi, A., Castellino, F., Bonifacio, E., Del Pap, B., Tiziana, Z., Iacucci Ostini, R., Cecchini, D., Aloisi, T., Perruccio, K., Ruggeri, L., Balucani, C. Pierini, A., Sportoletti, P., Aristei, C., Falini, B., Reisner, Y., Verlardi, A., Aversa, F., and Martelli, M.F.

Blood (2011) April 7; 117(14): 3921-3928.

Cord Blood Transplantation

Optimization of cGMP purification and expansion of umbilical cord blood-derived T-regulatory cells in support of first-in-human clinical trials

McKenna JR. DH., Sumstad D., Kadidlo D.M., Batdorf B., Lord C.J., Merkel S.C., Koellner C.M., Curtsinger J.M., June C.H., Riley J. L., Levine B., Miller J. S., Brunstein C. G., Wagner J. E., Blazar B. R., Hippen K. L. Cytotherapy (2017) Feb., Vol 19,p 250–262

Umbilical cord blood-derived T regulatory cells to prevent GVHD: kinetics, toxicity profile and clinical effect

Brunstein CG, Miller JS, McKenna DH, Hippen KL, DeFor TE, Sumstad D, Curtsinger J, Verneris MR, MacMillan ML, Levine BL, Riley JI, June CH, Le C, Weisdorf D, McGlave PB, Blazar BR, Wagner JE. Blood. (2015) Nov 12. epub

Infusion of ex vivo expanded T regulatory cells in adults transplanted with umbilical cord blood: safety profile and detection kinetics.

Brunstein, C.G., Miller, J.S., Cao, Q., McKenna, D.H., Hippen, K.L., Curtsinger, J., DeFor, T., Levine, B.L., June, C.H., Rubinstein, P., McGlave, P.B., Blazar, B., and Wagner, J.E. Blood (2011) Jan 20; 117(3): 1061-1070.

Autoimmune Diseases

Preparation of functionally preserved CD4+CD25high regulatory T cells from leukapheresis products from ulcerative colitis patients, applicable to regulatory T-cell transfer therapy.

Sumida, Y., Nakamura, K., Kanayama, K., Akiho, H., Teshima, T., and Takayanagi, R.
Cytotherapy (2008) 10(7): 698-710.

Inability to mediate prolonged reduction of regulatory T Cells after transfer of autologous CD25-depleted PBMC and interleukin-2 after lymphodepleting chemotherapy.

Powell, D.J. Jr., de Vries, C.R., Allen, T., Ahmadzadeh, M., and Rosenberg, S.A.
J. Immunother. (2007) May-Jun; 30(4): 438-47.

CD25 Depletion

Performance data

A phase I study of CD25/regulatory T-cell-depleted donor lymphocyte infusion for relapse after allogeneic stem cell transplantation. Nikiforow S., Kim H. T., Daley H., Reynolds C., Jones K. T., Armand P., Ho V. T., Alyea E. P., Cutler C.S., Ritz J., Antin J.H., Soiffer R.J., Koreth J.
Haematologica (2016) Oct; 101: 1251-1259

Optimization of methodology for production of CD25/CD71 allodepleted donor T cells for clinical use.

Albon SJ, Mancao C, Gilmour K, White G, Ricciardelli I, Brewin J, Lugthart G, Wallace R, Amrolia PJ.
Cytotherapy (2013) Jan;15(1):109-21

Large-scale depletion of CD25+ regulatory T cells from patient leukapheresis samples.

Powell, D.J. Jr., Parker, L.L., and Rosenberg, S.A.
J. Immunother. (2005) Jul-Aug; 28(4): 403-11.

CD25+ Regulatory T CELL-Depleted DONOR Lymphocyte Infusion for Relapse After Allogeneic Transplantation – A PHASE 1 Study

Nikiforow S. Kim H. Kao G., Sainvil M.-M., McDonough S.M., Armand P., Ho V.T., Alyea E.P., Cutler C., Ritz J., Antin J.H., Soiffer R.J., Koreth J.
ASBMT Meeting (2013), oral presentation

CD4+CD25+ Regulatory T Cell Depletion Improves the Graft-Versus-Tumor Effect of Donor Lymphocytes After Allogeneic Hematopoietic Stem Cell Transplantation.

Maury, S., Lemoine, F.M., Hicherie, Y., Rosenzweig, M., Badoual, C., Cherai, M., Beaumont, J.-L., Azar, N., Dhedin, N., Sirvent, A., Buzyn, A., Rubio, M.-T., Vigouroux, S., Montagne, O., Bories, D., Roudot-Thoraval, F., Vernant, J.-P., Cordonnier, C., Klatzmann, D., and Cohen, S.J.
Sci. Transl. Med. (2010) Jul 21; 2(41): 41ra52.

Adoptive transfer of T(reg) depleted autologous T cells in advanced renal cell carcinoma.

Thistlethwaite, F.C., Elkord, E., Griffiths, R.W., Burt, D.J., Shablak, A.M., Campbell, J.D., Gilham, D.E., Austin, E.B., Stern, P.L., and Hawkins, R.E.
Cancer Immunol. Immunother. (2008) May; 57(5): 623-34.



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