(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
31 May 2019 (31.05.2019)

WIPO | PCT

(10) International Publication Number
WO 2019/101773 A2

(51) International Patent Classification:
Not classified

(21) International Application Number:
PCT/EP2018/082022

(22) International Filing Date:
21 November 2018 (21.11.2018)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
17203527.1 24 November 2017 (24.11.2017) EP
18191954.9 31 August 2018 (31.08.2018) EP

(71) Applicant: **DEFENSIN THERAPEUTICS APS** [DK/DK]; c/o COBIS Ole Maaløes Vej 3, 2200 Copenhagen N (DK).

(72) Inventor: **NORDKILD, Peter**; Vældegaardsvej 59, 2820 Gentofte (DK).

(74) Agent: **HØIBERG P/S**; Adelgade 12, 1304 Copenhagen K (DK).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(54) Title: PREVENTION AND TREATMENT OF GRAFT-VERSUS-HOST-DISEASE WITH DEFENSINS

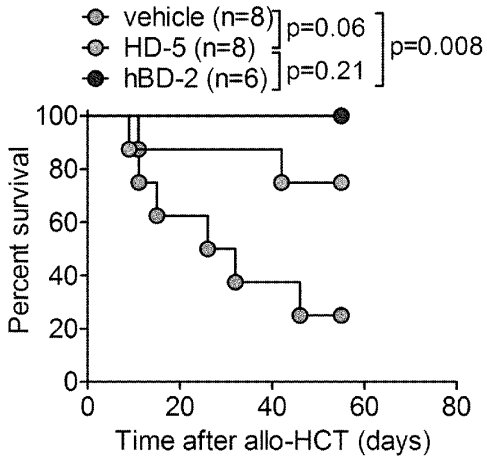


Fig 58

(57) Abstract: The present invention relates to methods for treatment and/or prevention of acute as well as chronic graft-versus-host-disease (GVHD), and in particular to methods for decreasing mortality and increasing especially long term survival; acute complications associated with GVHD such as diarrhoea, weight loss and sepsis based on normalization of gut, liver, lung and skin microbiota and mucosal defense; rebalance of the immune system with normalization of cytokine production of IFN-γ, TNF-α, 11-4, IL- 5, IL-6, IL-8, IL-9, IL-10 and IL-13 and prevention and/or treatment of cytokine storm; chronic complications associated with GVHD such as bronchiolitis obliterans and scleroderma, the method comprising oral, subcutaneous, intrapulmonary and/or dermal/transdermal administration of one or more mammalian defensins selected from the group of α- and β-defensins in a patient that has or is about to receive an allogeneic hematopoietic stem cell transplantation.

WO 2019/101773 A2

[Continued on next page]

(84) **Designated States** *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— *of inventorship (Rule 4.17(iv))*

Published:

— *without international search report and to be republished upon receipt of that report (Rule 48.2(g))*

— *with sequence listing part of description (Rule 5.2(a))*