

## Supplementary Material

### Efficacy and safety of fast-acting insulin aspart in people with type 1 diabetes using carbohydrate counting: a *post hoc* analysis of two randomised controlled trials

Rose L, Kadowaki T, Pieber TR, Buchholtz K, Ekelund M, Gorst-Rasmussen A, Philis-Tsimikas A

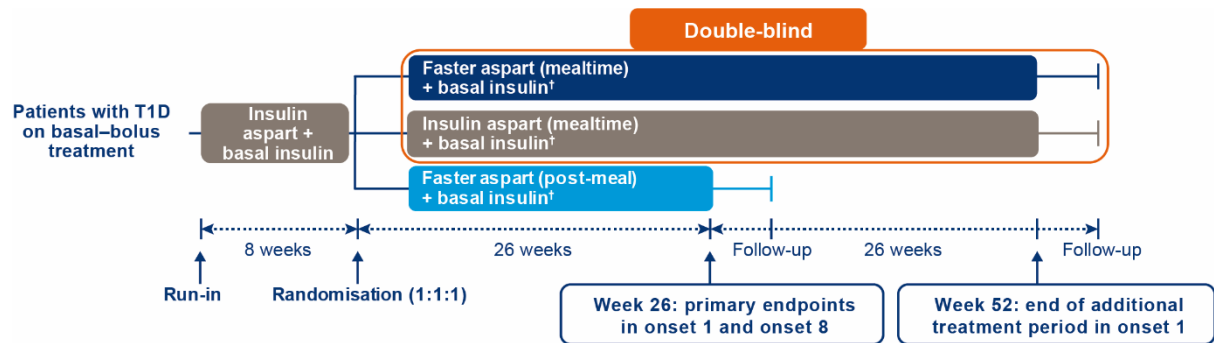
**Table S1. Bolus dose titration algorithm**

| Pre-prandial glucose (mmol/L) | Dose adjustment (U) | Rules for dose adjustments                    |
|-------------------------------|---------------------|---|
| <4.0                          | -1                  | ≥1 SMBG below target                          |
| 4.0–6.0                       | No adjustment       | 0–1 SMBG above target<br>No SMBG below target |
| >6.0                          | +1                  | ≥2 SMBG above target<br>No SMBG below target  |

Adjustments were made twice weekly, once by the investigator and once by the participant.

SMBG, self-measured blood glucose; U, units.

**Fig. S1:** Trial design of onset 1 and onset 8



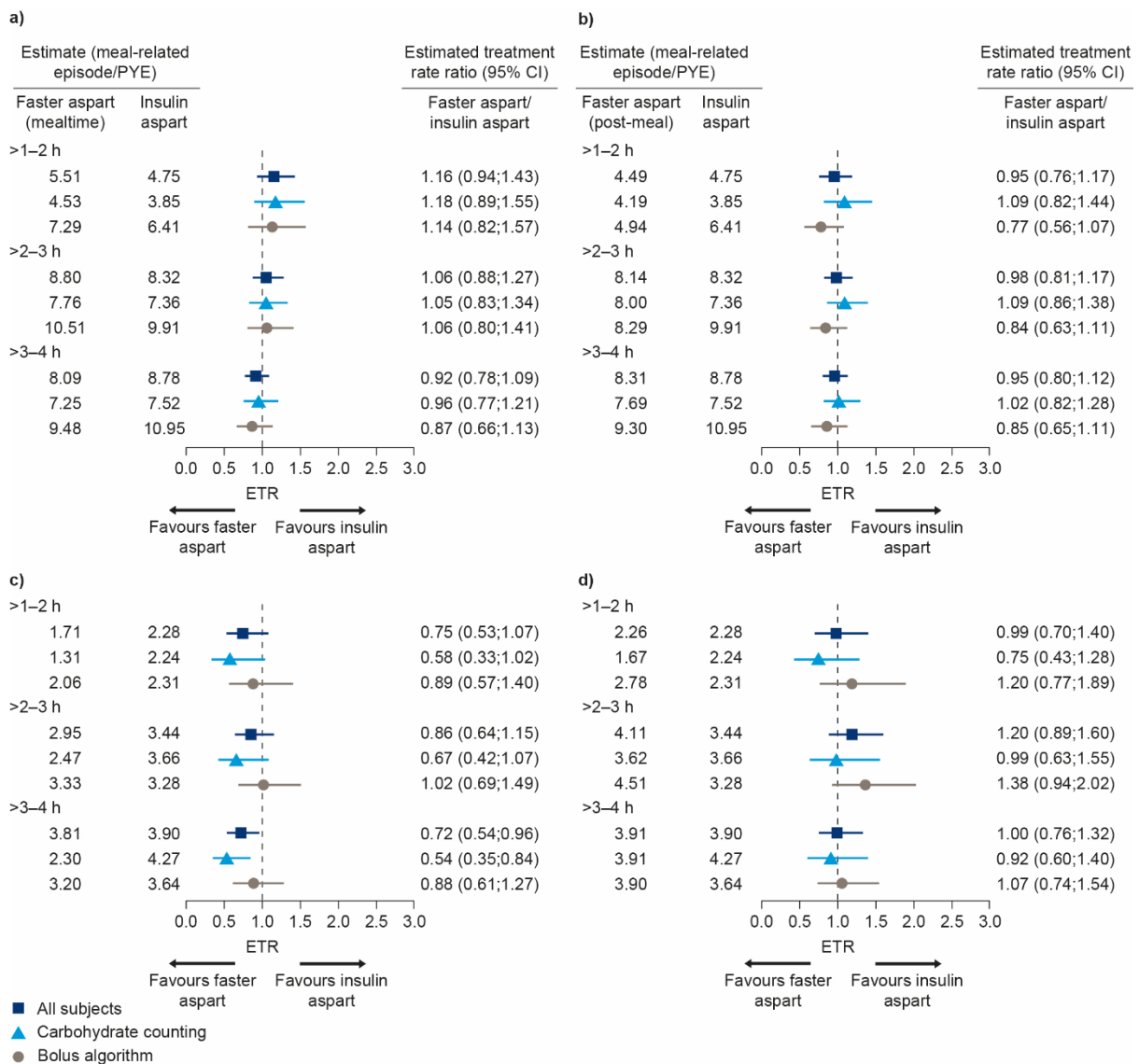
†Insulin detemir in onset 1 and insulin degludec in onset 8.

ClinicalTrials.gov: NCT01831765 (onset 1) and NCT02500706 (onset 8). Baseline is at randomisation.

Follow-up was at 7–30 days. Change from baseline in HbA1c at week 26 was the primary endpoint in both onset 1 and onset 8. An additional 26-week treatment period was included in onset 1 to document long-term safety (data not included in the *post hoc* analysis).

Faster aspart, fast-acting insulin aspart; T1D, type 1 diabetes.

**Fig. S2:** Non-cumulative meal-related severe or BG-confirmed hypoglycaemia rates after 26 weeks for a) mealtime and b) post-meal faster aspart in onset 1, and c) mealtime and d) post-meal faster aspart in onset 8, all versus insulin aspart, by dose adjustment method.



Non-cumulative rates of meal-related hypoglycaemia were evaluated during the >1-2, >2-3 and >3-4 h periods after the start of a meal. Data from 'all subjects' in each trial are included alongside data from the dose adjustment method groups.

CI, confidence interval; ETR, estimated treatment ratio; faster aspart, fast-acting insulin aspart; PYE, patient-year of exposure.

## Supplementary Appendix

### onset 1 independent ethics committees/institutional review boards

**Belgium:** Ethics Committee UZA, Edegem; Ethics Committee Erasme-ULB, Brussels; Commissie Medische Ethiek van de Universitaire Ziekenhuizen K.U. Leuven, Leuven; Ethics Committee UZ Gent, Gent; Imelda vzw Commissie Medisch Ethiek, Bonheiden. **Canada:** Comité d'éthique de la Recherche - Institut de Recherches Cliniques de Montreal, Montreal, QC; University of Alberta, Research Ethics Office, Health Research Ethics Board, Edmonton, AL; Hamilton Integrated Research Ethics Board (HIREB), Hamilton, ON; Institutional Review Board (IRB) Services, Aurora, ON; The University of Manitoba, Biomedical Research Ethics Board, Winnipeg, MB; Comité d'éthique de la recherche CHU de Québec – Université Laval, Quebec, QC; Western University Health Science Research Ethics Board, London, ON; Mount Sinai Hospital Research Ethics Board, Toronto, ON; Health Research Ethics Board of Alberta, Clinical Trials Committee, Edmonton, AB; Vancouver Island Health Authority Research Ethics Board, Victoria, BC; Institutional Review Board (IRB) Services, Aurora, ON. **Czech Republic:** Multicentrická Etická komise Fakultní nemocnice u Sv. Anny v Brně, Brno; Etická komise IKEM a FTNSP (Fakultní Thomayerova nemocnice s poliklinikou), Prague; Etická komise Fakultní nemocnice Hradec Králové, Hradec Králové; Etická komise pro multicentrická klinická hodnocení, Etická komise VFN, Prague. **Finland:** Helsinki and Uusimaa Hospital District Ethics Committee, Department of Medicine Biomedicum Helsinki 2C, Helsinki. **Germany:** Ethikkommission der Ärztekammer Westfalen-Lippe und der Medizinischen Fakultät der Westfälischen Wilhelmsuniversität, Muenster. **Hungary:** Medical Research Council Ethics Committee for Clinical Pharmacology, Budapest. **Poland:** Komisja Bioetyczna przy Okregowej Izbie Lekarskiej w Bialymstoku, Bialystok. **United Kingdom:** NRES Committee London – South East Bristol REC Centre, Bristol. **United States:** Sterling Institutional Review Board, Atlanta, GA; Veterans Affairs Institutional Review Board, Lexington, KY; Christiana Care Institutional Review Board, Newark, DE; University of Texas Southwestern Medical Center at Dallas Institutional Review Board, Dallas, TX; Western Institutional Review Board, Puyallup, WA;

Icahn School of Medicine at Mount Sinai Institutional Review Board, New York, NY; University of North Carolina Office of Human Research Ethics, Chapel Hill, NC; Johns Hopkins Institutional Review Board, Baltimore, MD; Park Nicollet Institute Institutional Review Board, Minneapolis, MN; Baylor Research Institute Institutional Review Board, Dallas, TX; Chesapeake Institutional Review Board, Columbia, MD; Oregon Health & Science University Research Integrity Office, Portland, OR; University of Miami Human Subjects Research Office, Miami, FL; St. Luke's Health System Institutional Review Board, Boise, ID; Washington State University Institutional Review Board, Pullman, WA; Rochester General Health Systems IRB, Rochester, NY; UMass Medical School IRB, The Committee for Protection of Human Subjects in Research, Worcester, MA; Edward Hines Jr. VA Hospital/Captain James A. Lovell Federal Health Care Center Institutional Review Board, Hines, IL

#### **onset 8 independent ethics committees/institutional review boards**

**Austria:** Ethikkommission der Stadt Wien TownTown, Wien; Ethikkommission der Medizinischen Universität Graz, Graz; EK für das Bundesland Salzburg, Salzburg. **Bulgaria:** Ethics Committee for Multicentre Clinical Trials, Sofia. **Canada:** Comité d'éthique de la Recherche - Institut de Recherches Cliniques de Montréal, Montreal, QC; Nova Scotia Health Authority Research Ethics Board, Halifax, NS; Health Research Ethics Board of Alberta Clinical Trials Committee, Edmonton, AL; Comité d'Éthique de la Recherche de l'IUCPQ-Université Laval, Quebec, QC; Institutional Review Board Services, Aurora, ON. **Germany:** Landesärztekammer Brandenburg Ethikkommission, Cottbus. **Israel:** Hadassah Helsinki Committee, Jerusalem; Rabin Helsinki Committee, Petah-Tikva; Rambam Helsinki Committee, Haifa; Assuta Helsinki Committee, Tel Aviv; Wolfson Helsinki Committee, Holon; Meir Helsinki Committee, Kfar Saba. **India:** Institutional Ethics Committee, Ramdevrao Hospital, Kukatpally; Institutional Review Board, Christian Medical College, Vellore; Madras Diabetes Research Foundation Institutional Ethics Committee, Chennai; Institutional Ethics Committee, Govt. Medical College, Kozhikode, Kerala; Institutional Ethics Committee, Poona Medical Research Foundation, Pune; Institute Ethics Committee, AIIMS, New Delhi; Cuttack Diabetes Research Foundation Ethics

Committee, Pune; KEM Hospital and Research Centre, Ethics Committee, Pune; Multispeciality Ethics Committee, Mithakhali, Ellisbridge, Ahmedabad; Sterling Hospital Ethics Committee, Ahmedabad; Integrity Ethics Committee, Convenient Hospitals, Chennai; Ethics Committee, Prof. M. Viswanathan Diabetes Research Institute, Chennai; Ethics Committee, PT. Sharma UHS, Institutional Rohtak, Haryana; PGIMER, Institutional Ethics Committee, Chandigarh; Institutional Ethics Committee, King George Hospital, Visakhapatnam; Ethics Committee of Diabetes Thyroid Hormone Research Institute, BCM Health Island, Indore. **Italy:** COMITATO ETICO DELL'IRCCS FONDAZIONE S. RAFFAELE DEL MONTE TABOR DI MILANO, Milan; COMITATO DI BIOETICA DELLA.O. Papa Giovanni XXIII, Bergamo; Comitato Etico Policlinico Universitario "Agostino Gemelli", Rome; COMITATO ETICO DELL'AZIENDA OSPEDALIERO UNIVERSITARIA OSPEDALI RIUNITI UMBERTO I - G.M. LANCISI - G. SALESI DI ANCONA, Ancona; COMITATO ETICO REGIONE CALABRIA sez. Area Centro, Catanzaro; Comitato Etico IRCCS MultiMedica Sezione del Comitato Etico Centrale IRCCS Lombardia, Sesto San Giovanni. **Japan:** Kojin-kai Sapporo Dermatology Clinic IRB, Hokkaido; Iryo Houjin Manda Memorial Hospital IRB, Hokkaido; Kojin-kai Sapporo Dermatology Clinic IRB, Hokkaido; Seino Clinic IRB, Fukushima; Iryo Houjin Kenseikai NAKAKINEN CLINIC IRB, Naka; Clinic of the Institute for Adult Diseases Asahi Life Foundation IRB, Tokyo; H. E. C Science Clinic IRB, Yokohama; Nihonbashi Sakura Clinic IRB, Tokyo; Takatsuki Red Cross Hospital IRB, Osaka; Nakameguro Atlas Clinic IRB, Tokyo; Osaka City University Hospital IRB, Osaka; Iryohojinshadan Sinwakai Adachi, Tokyo; Iryo Houjin Shadan Jinnouchikai Jinnouchi Hospital IRB, Kumamoto; Nihonbashi Sakura Clinic IRB, Tokyo; Iryo Houjin Shadan Kowakai Heiwadai Hospital IRB, Miyazaki; The Jikei University Hospital IRB, Tokyo; Shinshu University Hospital IRB, Nagano; Tokyo Women's Medical Hospital IRB, Tokyo; Juntendo University Hospital IRB, Tokyo; Tokai Kinen Hospital IRB, Aichi; Shin-Koga Hospital IRB, Fukuoka; JCCR-IRB, Tokyo. **Serbia:** Committee Clinical Centre of Serbia, Belgrade. **Russian Federation:** Ethics Committee at Ministry of Health of the Russian Federation, Moscow; Local Ethics Committee of St. Petersburg GUZ "City St. Elizabeth Hospital", Saint-Petersburg; Ethics Committee of the SBEI APE Russian Medical Academy of Postgraduate Education, Moscow; Ethics Committee of "Astarta" LLC,

Saint-Petersburg; Local Ethics Committee of Federal State Budgetary Scientific Institution "Research Institute of Clinical and Experimental Lymphology", Novosibirsk; Local Ethics Committee of SHI Regional Clinical Hospital, Saratov; Local Ethics Committee of St. Petersburg State Medical University n.a. I.P. Pavlov of MoH of Russia, Saint-Petersburg; Ethics Committee of Regional State Budgetary Healthcare Institution "City Hospital #5 of Barnaul town", Barnaul; Ethics Committee of the State Budgetary Educational Institution of Highest Professional Education "First Moscow State Medical University named after I.M. Sechenov" of the Ministry of Health of Russian Federation, Moscow; Ethics Committee of State Budget Educational Institution of Higher Professional Education "Novosibirsk State Medical University" of the Ministry of Healthcare of Russian Federation, Novosibirsk; Ethics Committee of Tyumen State Medical Academy, Tyumen; Ethics Committee of State Budgetary Educational Institution of Additional Professional Education "Kazan State Medical Academy" of Ministry of Health of Russian Federation, Kazan. **Taiwan:** Cheng Hsin General Hospital Institutional Review Board, Taipei; Mackay Memorial Hospital Institutional Review Board, Taipei City; Chang Gung Medical Foundation Institutional Review Board, Taipei. **United States:** Sterling Institutional Review Board, Atlanta, GA; Park Nicollet IRB HealthPartners Institute, Bloomington, MN; Office of Human Research Ethics, Chapel Hill, NC; Rochester Regional Health Clinical Investigation Committee, Rochester, NY; Western Institutional Review Board, Olympia, WA