Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

eAppendix 1. List of Investigators and Corresponding Author; Trial Sites and Institutions of Authors; EMERGE Steering Group; Data and Safety Monitoring Committee

List of Investigators and Corresponding Author

[1,2,3] Professor Fidelma Dunne PhD

[1,2 3] Dr Christine Newman MD

[2]Dr Alberto Alvarez-Iglesias PhD

[2]Dr John Ferguson PhD

[1,2,3] Professor Andrew Smyth PhD

[2]Dr Marie Browne PhD

[1]Dr Paula O'Shea PhD

[1,2]Professor Declan Devane PhD

[7]Professor Paddy Gillespie PhD

[1,2,4] Dr Delia Bogdanet PhD

[1,5] Dr Oratile Kgosidialwa MD

[1,8]Professor Aoife Egan PhD

[1,2,3] Dr Yvonne Finn MD

[1,2,3] Dr Geraldine Gaffney MD

[2]Dr Aftab Khattak MD

[1,2,3] Professor Derek O'Keeffe PhD

[1,6] Professor Aaron Liew PhD

[1,2,3] Professor Martin O Donnell PhD

Corresponding investigator:

Professor Fidelma Dunne

Fidelma.dunne@universityofgalway.ie

Room 1005, Clinical Science Institute, University of Galway, Galway, H91 V4AY, Ireland

Trial Sites and Institutions of Authors

College of Medicine Nursing and Health Sciences University of Galway[1]

Clinical Research Facility, University of Galway[2]

Galway University Hospital[3] Newcastle Road, Galway Ireland

Mayo University Hospital[4] Westport Road, Castlebar Co Mayo Ireland

Cork University Hospital[5] Wilton Road, Cork Ireland

Portiuncula University Hospital[6]Portiuncula, Co Galway Ireland

School of Business and Economics[7], University of Galway

Mayo Clinic[8] Rochester Minnesota USA

EMERGE Steering Group

Fidelma Dunne

Andrew Smyth

Martin O Donnell

Declan Devane

Alberto Alvarez-Iglesias

Marie Browne

Karolina Rokita-Loughman

Oleskii Noreiko

Sinead Gill

Sinead Wallace

Kevin Normoyle

Javkar Padmya

Data and Safety Monitoring Committee

Peter Damm

Fiona Boland

Carl Scarrott

Eoin Noctor

eBox. Contraindications to the Use of Metformin Excluding Women From EMERGE Trial

- renal insufficiency (serum creatinine >130 µmol/L or creatinine clearance <60ml/min),
- moderate to severe liver dysfunction (aspartate aminotransferase (AST) or alanine aminotransferase (ALT) > three times the upper limit of normal),
- shock or sepsis at recruitment,
- previous hypersensitivity to metformin,
- known foetal anomaly,
- known small for gestational age (SGA) (foetal growth <10^{th} percentile),
- known gestational hypertension, preeclampsia, ruptured membranes,
- history of significant drug or alcohol use,
- history of significant gastrointestinal problems such as severe vomiting, Crohn's disease and colitis which will inadvertently affect the absorption of the study drug,
- congestive heart failure or a history of congestive heart failure,
- serious mental illness
- hereditary problems of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption.

eAppendix 2. Usual Care of Women With GDM

In our trial sites, usual care for women with GDM consists of information on medical nutritional therapy (MNT) provided by a dietitian and information on appropriate exercise provided by members of the multi-disciplinary team. These lifestyle measures are commenced within 1 week of a diagnosis. At the same time the diabetes specialist nurse or midwife instructs the woman on the use of a glucometer and each woman is instructed to perform 7-point glucose testing before and 1 hour post meals and at bedtime. Women are reviewed every 2-4 weeks in a joint obstetric diabetes antenatal clinic and receive additional telephone support between clinic visits as required. Literature on GDM and management are also given to women. If insulin is required, the woman meets the diabetes nurse or midwife who discusses the insulin types and frequency to be used. They are educated on dealing with low and high glucose measurements including use of a glucagon pen. At each clinic visit, the weight and blood pressure are checked and urinalysis completed. A glycated haemoglobin is assessed every 4 weeks. Ultrasound scanning occurs every 4 weeks for foetal growth and mode of delivery is individualised and documented taking in to consideration foetal health and growth, maternal health and previous delivery type. Following delivery insulin is discontinued and usual diet and lifestyle resumed. Breastfeeding is encouraged. Prior to discharge women are scheduled for a repeat 75g OGTT at 12 weeks post-partum.

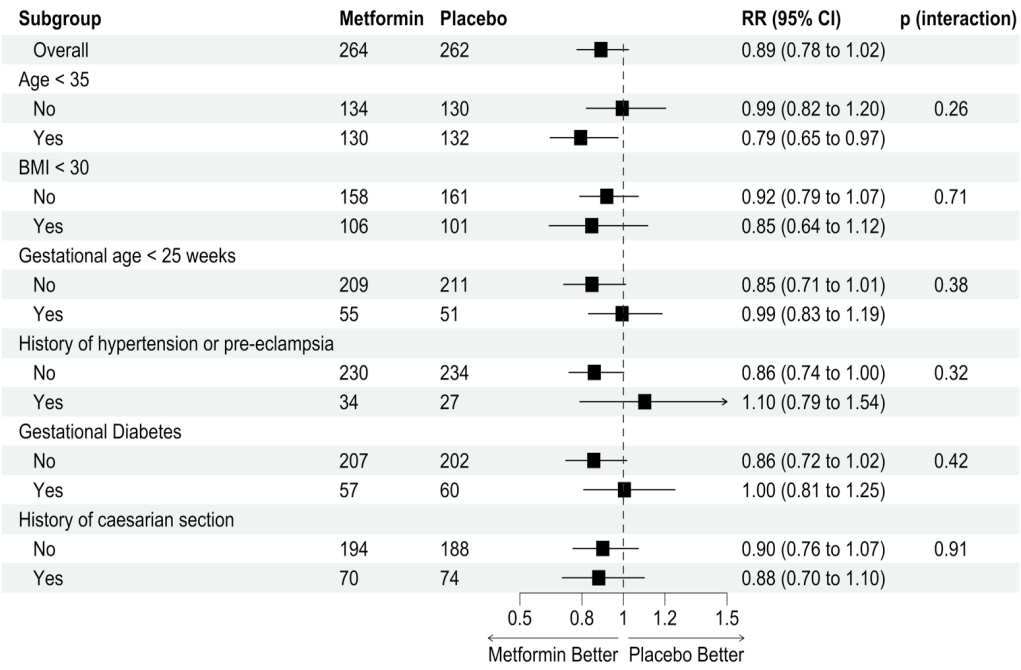
eTable 1. List of Variables Collected at Delivery and at 4 and 12 Weeks Postpartum

Delivery Visit	4 week postpartum	12 weeks postpartum
Maternal BP Maternal Pulse Maternal Adverse events Infant Adverse events Delivery date Mode of delivery Delivery complications Feeding method initiated Infant sex Infant weight Crown-heel measurement Upper arm circumference Abdominal circumference Head circumference Apgar score at 5 mins Neonatal Hypoglycaemia Neonatal jaundice Respiratory distress NICU	Discharge date Current health status of baby Current feeding method Neonatal morbidity since discharge Adverse events –maternal Adverse events-baby EQ5D-5L questionnaire Rowan questionnaire	Maternal BP, pulse, weight, BMI and waist circumference 75gOGTT Lipids insulin and c peptide EQ5D-5L questionnaire Current feeding method Adverse events-mother Adverse events –baby Current health status of baby Neonatal morbidities

eTable 2. Neonatal and Maternal Morbidity

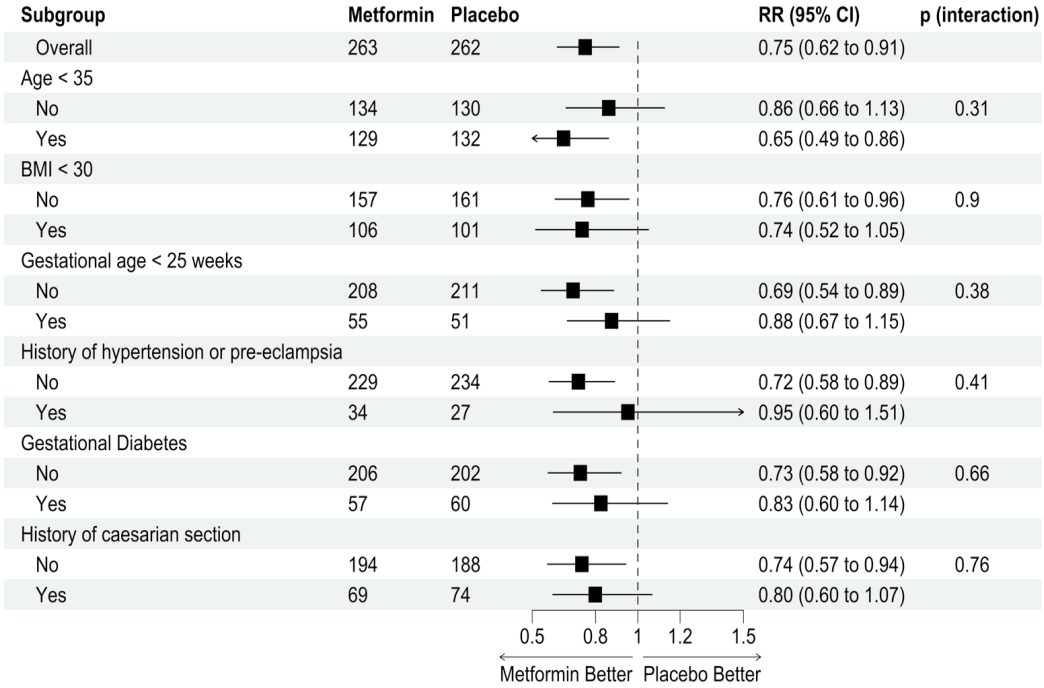
Maternal Morbidity	**Metformin % (n)**	**Placebo % (n)**	**RR (95% CI)**	**P value**
Antepartum haemorrhage Post-partum haemorrhage **Any bleeding**	5.7% (15/262) 19.5% (51/262) 22.9% (60/262)	10.3% (27/262) 24.0%(63/262) 30.4% (80/262)	0.56 (0.3,1.02) 0.81 (0.59,1.13) 0.75 (0.56,1)	0.08 0.25 0.06
Gestational hypertension Preeclampsia	11.8% (31/262) 3.8% (10/262)	10.6% (28/262) 1.9% (5/262)	1.11 (0.69,1.8) 2.01 (0.7,5.79)	0.77 0.29
Induction of labour %(n)	28.6% (75/262)	33.5% (88/262)		0.37
Total Caesarean births	43.5% (114/262)	38% (100/262)		0.37
Elective Caesarean births	53.5% (61/114)	53.0% (53/100)		1
Emergency Caesarean births	46.5% (53/114)	47.0% (47/100)		1
Infection pre-natal Infection post-natal	2.6%(7/262) 7.3%(19/262)	3.0% (8/262) 12.5% (33/262)	0.88 (0.32, 2.39) 0.58 (0.34,0.99)	1 0.06
Exclusive breast feeding-delivery	45.8% (120/262)	48.9% (128/262)		0.17
Neonatal Morbidity				
Neonatal Hypoglycaemia	13.7% (36/262)	12.9% (34/262)	1.06 (0.69-1.64)	0.88
Respiratory Distress Syndrome (RDS)	9.2% (24/262)	6.8% (18/262)	1.34 (0.74-2.41)	0.41
Sepsis	0.4%(1/262)	1.1% (3/262)	0.33 (0.04-3.2)	0.62
Shoulder Dystocia	0.4%(1/262)	0.8% (2/262)	0.5 (0.05-5.46)	1
Jaundice needing Phototherapy	0.4%(1/262)	0	NA	1.00
Birth trauma	3.8%(10/262)	4.9% (13/262)	0.77 (0.34-1.73)	0.67
5-Min Apgar score <7 5-min mean Apgar score	0.4%(1/262) 9.2 (0.5)	0.4% (1/262) 9.1 (0.5)	1.0(0.0-15.9)	1.00 0.67
Major Congenital anomalies	3.8%(10/262)	2.7%(7/262)	1.43 (0.55-3.71)	0.62
Preterm birth (<37 wk of gestation) Iatrogenic PTB <37 weeks Spontaneous PTB < 37 weeks	9.2% (24/262) 5.0% (13/262) 4.2% (11/262)	6.5% (17/262) 3.4% (9/262) 3.1% (8/262)	1.41 (0.78, 2.57) 1.44 (0.63, 3.32) 1.37 (0.56,3.36)	0.33 0.51 0.64
Any NICU Admission NICU > 24-Hr stay	15.6% (41/262) 11.8% (31/262)	12.5% (33/262) 9.9% (26/262)	1.25 (0.82-1.91) 1.12 (0.73-1.96)	0.37 0.56

eFigure 1. Subgroup Analysis of the Primary Outcome



Legend: The primary composite outcome of insulin initiation or fasting glucose ≥ 5.1mmol/l at weeks 32 or 38 was consistent among subgroups

eFigure 2. Subgroup Analysis of Insulin Initiation Only



Legend: Insulin initiation alone was consistent among subgroups

eTable 3. Fasting (Laboratory) and Postprandial (Capillary) Glucose Values at Weeks 32 and 38 Between Groups

Meal	Metformin	Placebo	RR (95% CI)	P-Value
	Week 32			
Fasting	4.9 (0.5)	5 (0.5)	-0.19, -0.01	0.033
Breakfast	5.8 (1.2)	5.7 (1)		0.60
Lunch	5.5 (0.9)	5.7 (0.9)	-0.47, -0.04	0.02
Dinner	5.8 (1.1)	6 (1)		0.12
	Week 38			
Fasting	4.5 (0.4)	4.7 (0.5)	-0.28, -0.09	<0.001
Breakfast	5.4 (0.8)	5.7 (1)	-0.59, -0.04	0.024
Lunch	5.4 (0.9)	5.5 (0.9)		0.35
Dinner	5.5 (0.8)	6 (1)	-0.75,-0.25	<0.001