Methods Studies were performed on 125 infants <29 weeks gestation who required mechanical ventilation at 7–14 days and received 24 days of iNO at 20–2 ppm. A control group of 19 infants did not receive iNO.

Results In NO-treated infants there was a significant dose-dependent increase of both urinary NOx and cGMP per creatinine (maximal 3.1- and 2-fold, respectively, at 10–20 ppm iNO) compared to off iNO. The ratio of cGMP to NOx, which may reflect efficiency of NO signalling via guanylate cyclase, was lower (mean 38%) at all doses of iNO compared to off NO. NOx and cGMP concentrations at both 2 ppm and off iNO were inversely related to severity of lung disease (Respiratory Severity Score) during the first month, and the NOx levels were lower in infants who died or developed BPD at term. NOx was higher in Caucasian compared to other infants at all iNO doses.

Conclusions Urinary NOx and cGMP are biomarkers of endogenous NO production and lung uptake of NO, and levels at some doses reflect the severity of lung disease in infants. These results support a role of the NO-cGMP pathway in lung development and repair from injury.

Background Endothelin-1 (ET-1) is a potent pulmonary vasoconstrictor, involved in lung injury and remodelling. ET-1 can be estimated by measuring its stable by-product, C-terminal pro-ET-1 (CT-proET-1), in plasma.

Aims To investigate CT-proET-1 values in very preterm infants (gestational age <32 weeks) from birth to postmenstrual age (PMA) of 36 weeks, and their relationship with lung injury and bronchopulmonary dysplasia (BPD).

Methods Prospective cross-sectional study of 391 CT-proET-1 measurements (fully automated immunoflourescent assay) from 267 very preterm infants. Measurements were performed at birth (n = 72 infants), on day of life (DOL) 2 (n = 89), on DOL 6 (n = 49), on DOL 28 (n = 106), and at PMA 36 (n = 75). Trial registration: ClinicalTrials.gov NCT01644981.

Results CT-proET-1 values were (median) 151 pmoL/L (IQR 118–186) at birth, peaked on DOL 2 (319 pmoL/L (235–382)), and declined thereafter to 214 pmoL/L (148–293) on DOL 6, 184 pmoL/L (149–233) on DOL 28, and 150 pmoL/L (118–188) at PMA 36. Infants with BPD had higher CT-proET-1 values on DOL 2 (p = 0.001), DOL 6 (p < 0.001), and DOL 28 (p = 0.007), with no differences at birth and PMA 36 as compared to those without BPD. CT-proET-1 on DOL 6 was significantly correlated with days of mechanical ventilation, nasal CPAP, and oxygen requirement (Spearman’s Rs 0.637, 0.713, 0.745, respectively, p < 0.001 each). Moderate correlations were found for the same parameters on DOL 2 and DOL 28 but not for birth and PMA 36.

Conclusions The levels and the pattern of CT-proET-1 increase during the first week of life might serve as an early marker of BPD.