Monensin is a ionophor with a selecting capacity against Gram- rumen bacteria. In the overall, it increases the production of the rumen propionic acid and fosters liver gluconeogenesis. Previously, we observed that epithelial cells of the bovine forestomachs can recognize and respond differently to changes of rumen milieu and that cows show distinct tendencies to leukocyte infiltration into rumen fluids, in accordance to specific diets and dangerous fermentations (1). Considering the positive metabolic effects Monensin offered as rumen bolus during the transition period, we investigated its effects on rumen fermentations and innate immune responses of the forestomachs. On the whole, 43 cows (13 heifers and 30 multiparous) were allocated to two homogeneous groups: Kexx, which received 32.4 g of monensin by Controlled Release Capsule (Kexxtone®, Elanco Animal Health, UK) 21 days before expected calving, and Ctrl (control). Cows were frequently monitored during the transition period for health status, milk yield and quality, inflamo-metabolic profile (2). Moreover, individual rumen samples were collected with an oro-gastric probe at 30 days in milk (DIM), 6 hours after feed distribution. pH was measured immediately after withdrawal and rumen samples were collected with or without a cryoprotectant (fetal bovine serum and dimethyl sulfoxide). Samples were frozen at –80 °C for flow cytometry and molecular assays (CD45= total leukocytes; IL-A24 = granulocytes and monocytes; CD3 = T lymphocytes; sIgM = B lymphocytes; IGCL=Immunoglobulin light chain) and at -20 °C for volatile fatty acids (VFA) and ammonia. Rumen data were analyzed with ANOVA (SAS Inst. Inc., Cary, NC), considering the fixed effect of treatment and parity. As opposed to parity (not significant), treatment led to significant differences. Kexx cows at 30 DIM showed a similar pH (around 6.45), and lower concentration of ammonia (58.7 vs 93.3 mg/L of Ctrl; P< 0.05), a higher concentration of propionic acid (24.5 vs 22.4 mol/100 mol of Ctrl; P< 0.10, tendency) and a reduced acetoc:propionic ratio (2.5 vs 2.8 of Ctrl; P< 0.10, tendency). Moreover, Kexx vs Ctrl cows showed a lower number of B lymphocytes (1.66 vs 2.50%; P<0.01) and numerically lower amounts of immunoglobulins (IgM and total Ig) and T lymphocytes. The reduced prevalence of T lymphocytes was more marked in heifers receiving monensin (P< 0.10, tendency, vs Ctrl). On the whole, the activity of the innate immune system was more pronounced in the rumen of Ctrl cows, suggesting that monensin could have contributed to stabilize the rumen milieu and to attenuate the inflammatory responses that commonly occur in forestomachs around calving. These data were supported by clinical inspections (the significant lower incidences of diseases observed in the first two months of lactation) and metabolic data (lower NEFA and BOHB concentrations after calving) observed in the same Kexx cows (2). Our data confirm that nutritional and physiological changes in dairy cows can modify the innate immune response of forestomachs and that the evaluation of the rumen fluid can help evaluate animal health and welfare.