Supplementary Table 1. Overview of specimens with macroscopically evident lesions typical for foot-and-mouth disease (FMD) as well as mammary parenchyma taken for histologic examination and isolation of FMDV RNA.

| Cow | Sampling for histopathology | Sampling for RNA isolation (FFPE) |
|-----|------------------------------|----------------------------------|
| 1   | Mammary gland (right front qt. $n = 2$, left front qt. $n = 1$, right hind qt. $n = 2$), teat lesion (right and left front each $n = 2$), right udder lymph node ($n = 1$), muzzle ($n = 1$), tongue lesion ($n = 2$), interdigital skin lesion ($n = 2$) | Mammary gland ($n = 4$), teat lesion ($n = 4$), interdigital skin lesion ($n = 4$), tongue lesion ($n = 4$) |
| 2   | Mammary gland (right hind qt. $n = 2$, left hind qt. $n = 1$), teat lesion (right hind $n = 2$), left udder lymph node ($n = 1$), tongue ($n = 2$), hard palate lesion ($n = 1$), lip ($n = 1$) | Mammary gland ($n = 4$), teat lesion ($n = 2$), hard palate lesion ($n = 4$) |
| 3   | Mammary gland (left front qt. $n = 2$, right hind qt. $n = 1$), teat lesion (right hind $n = 2$), left udder lymph node ($n = 1$), muzzle ($n = 2$), tongue ($n = 1$), interdigital skin lesion ($n = 2$) | Mammary gland ($n = 4$), teat lesion ($n = 3$), interdigital skin lesion ($n = 4$), coronary band lesion ($n = 4$) |

FFPE = formalin-fixed, paraffin-embedded; qt. = quarter.
Supplementary Figure 1. Overview of lesions and virus detection by different methods. 1 = cow 1; 2 = cow 2; 3 = cow 3; FMDV = foot-and-mouth disease virus; IHC = immunohistochemistry; NE = not examined; neg = negative; pos = positive.; RT-qPCR = real-time quantitative PCR.

Supplementary Figure 2. Focal erosive and ulcerative thelitis at the apex of one or more teats was a consistent lesion in all 3 cows at autopsy.
Supplementary Figure 3. Detection of FMDV RNA in whole-milk samples. FMDV genome was detected until the end of the trial in all 3 cows. ND = not detected.

Supplementary Figure 4. Detection of FMDV RNA via RT-qPCR in samples of blood serum, saliva, and nasal secretion. FMDV genome could not be detected anymore in saliva, nasal secretion, and serum on day 12 post-infection. ND = not detected.