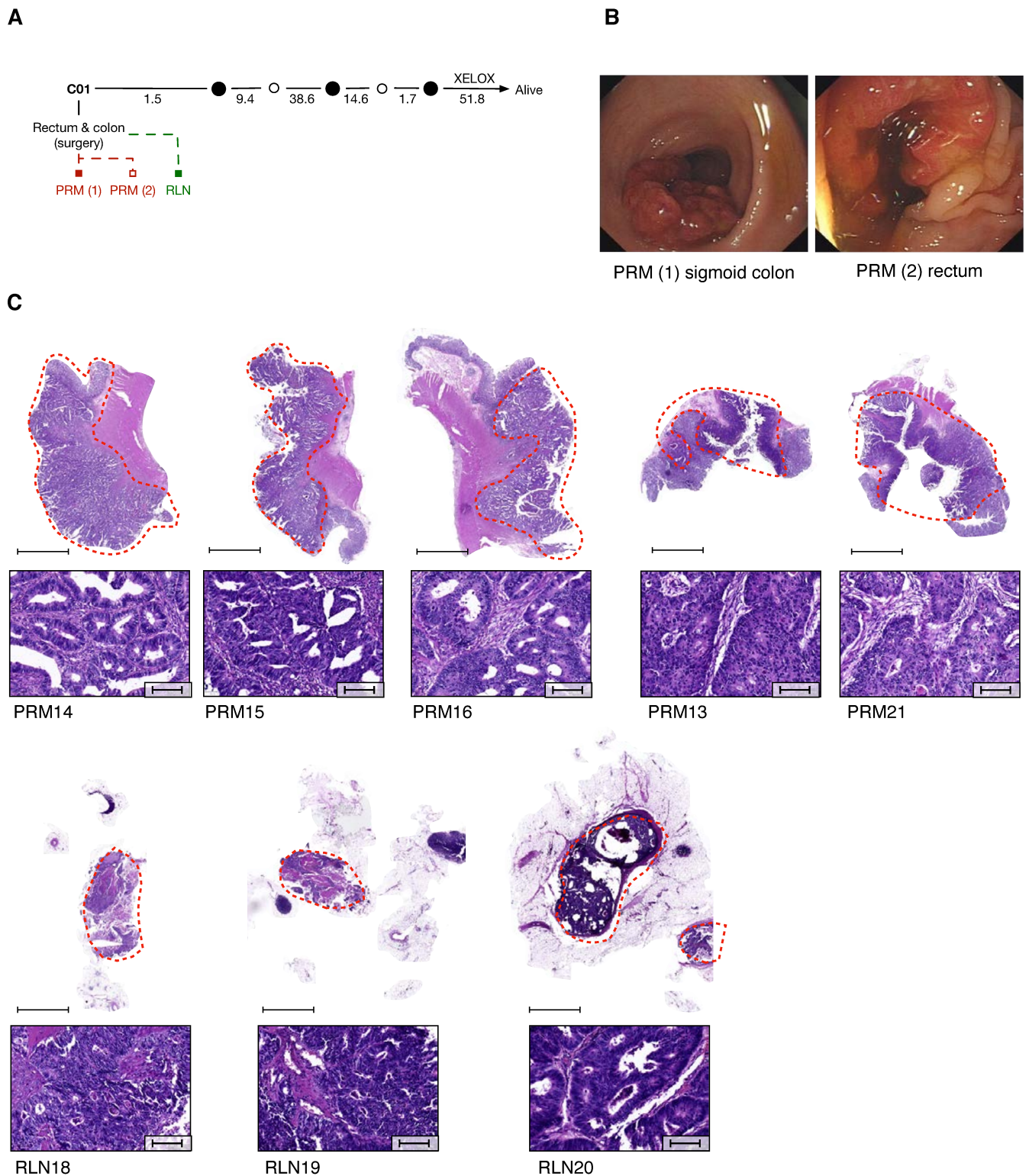
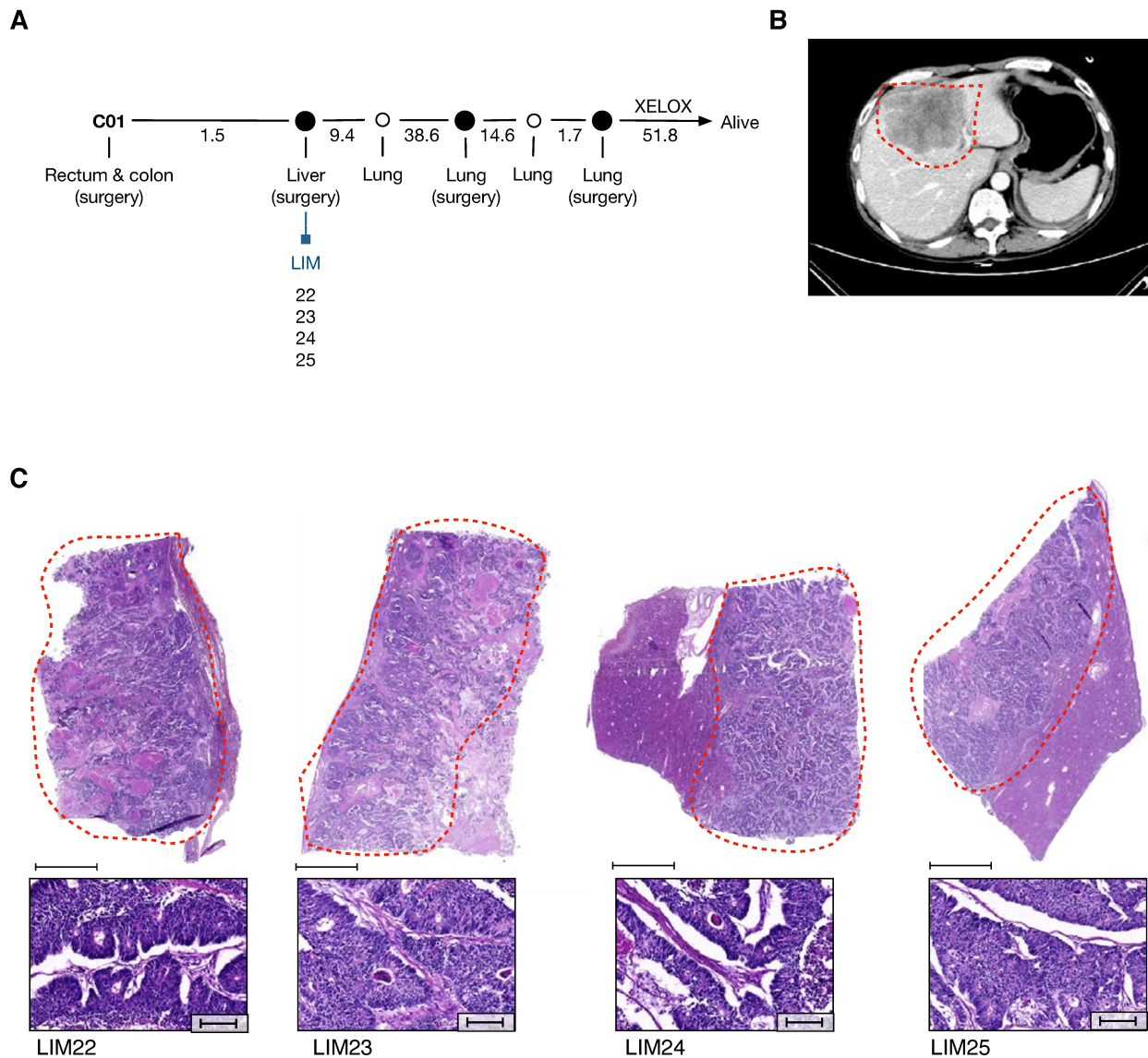


Data S1



Data S1-1. Pathological H&E evaluation of PRM and RLN in patient C01

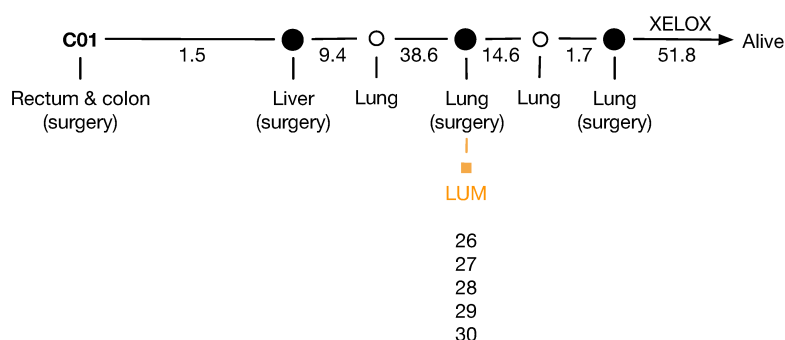
(A) Surgical time point of tumor resection; (B) Endoscopy pictures of two primary tumors in sigmoid colon and rectum; (C) PRM14, PRM15 and PRM16 were taken from a 2.5 cm × 2 cm × 0.8 cm polypoid mass which located at a distance of 1.0 cm from the distal end of the rectal mass. PRM13 and PRM21 were taken from a 3 cm × 2.5 cm × 1.0 cm ulcer-like mass located in a segment of the rectum. RLN18, RLN19 and RLN20 was taken from retrieved lymph node, diameter 1.0-2.5 cm. Tumorous region is marked by dashed red line; Scale bar for microscopic images, 100 μm; Scale bar for gross images, 5 mm.



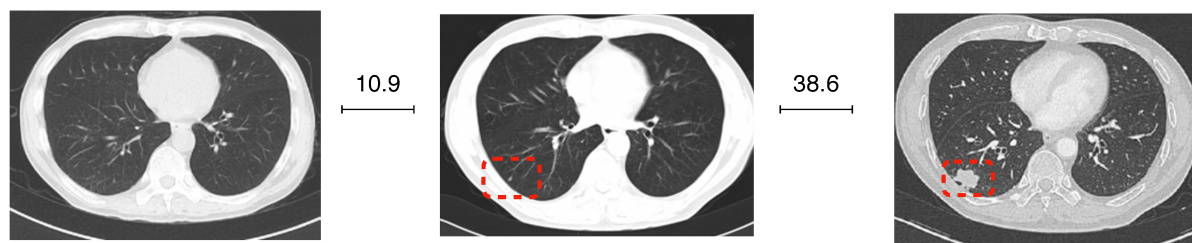
Data S1-2. Pathological H&E evaluation of LIM in patient C01

(A) Surgical time point of tumor resection; (B) CT imaging of liver metastasis; (C) A 14 cm x 9 cm x 7 cm nodular mass was surgically removed. LIM22 was taken from tumorous area close to the liver surface. LIM23 was taken from the tumor and liver capsule. LIM24 and LIM25 were taken from two sides of mass with peripheral liver tissue. Tumorous region is marked by dashed red line; Scale bar for microscopic images, 100 μ m; Scale bar for gross images, 5 mm.

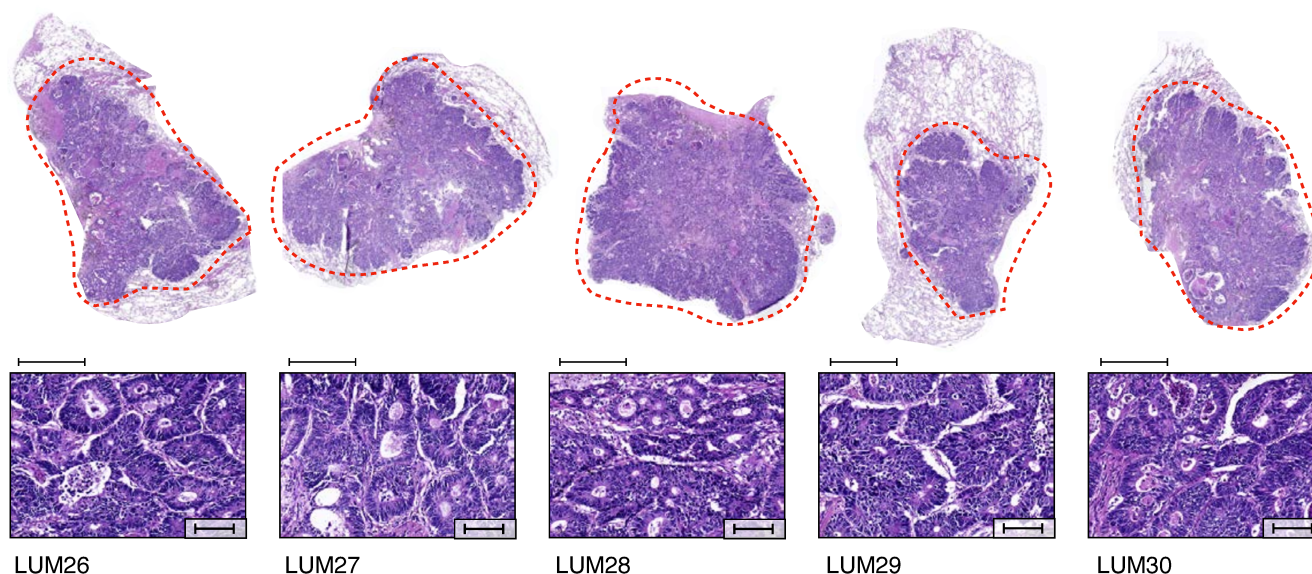
A



B



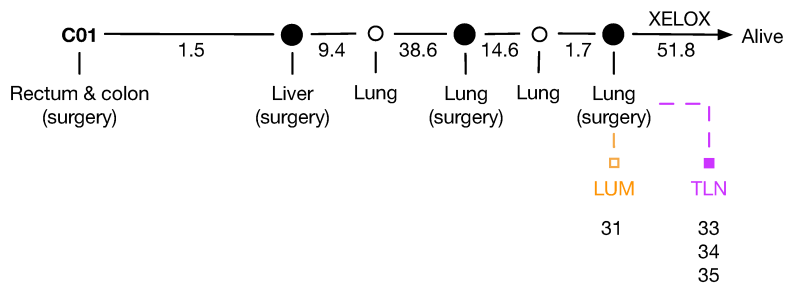
C



Data S1-3. Pathological H&E evaluation of LUM in patient C01

(A) Surgical time point of tumor resection; (B) CT imaging of lung metastasis. The same anatomical level of CT/MRI slice of metastatic event was demonstrated in rows across time points (months); (C) LUM26 to LUM30 was selected from the right lung metastasis. A 4.5 cm × 2.8 cm × 1.8 cm nodular mass was surgically removed. LUM26, LUM27 and LUM28 were taken from the mass nearby pleura. LUM29 was taken from the mass with surrounding lung tissue, while LUM30 was taken from the tumor inside. Tumorous region is marked by dashed red line; Scale bar for microscopic images, 100 μm; Scale bar for gross images, 5 mm.

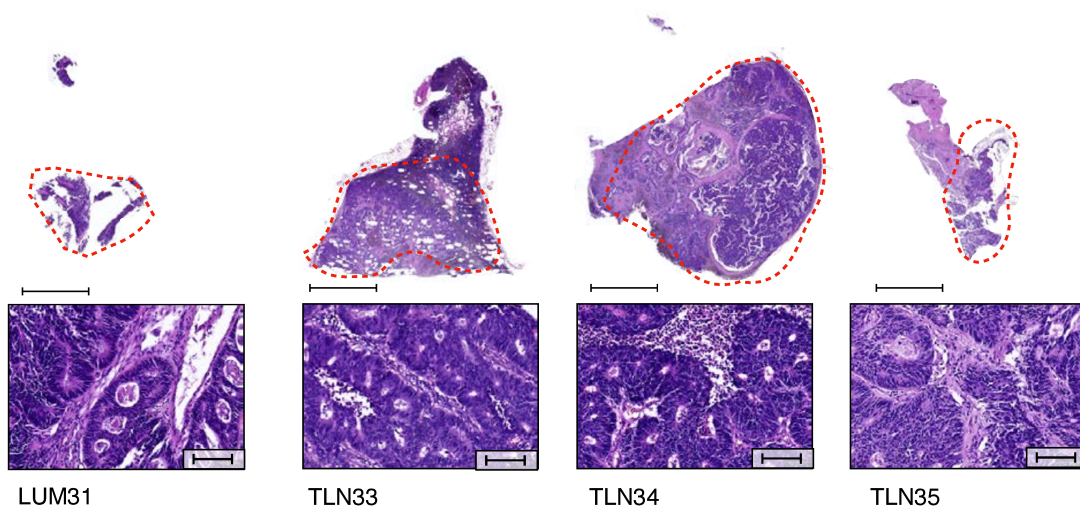
A



B

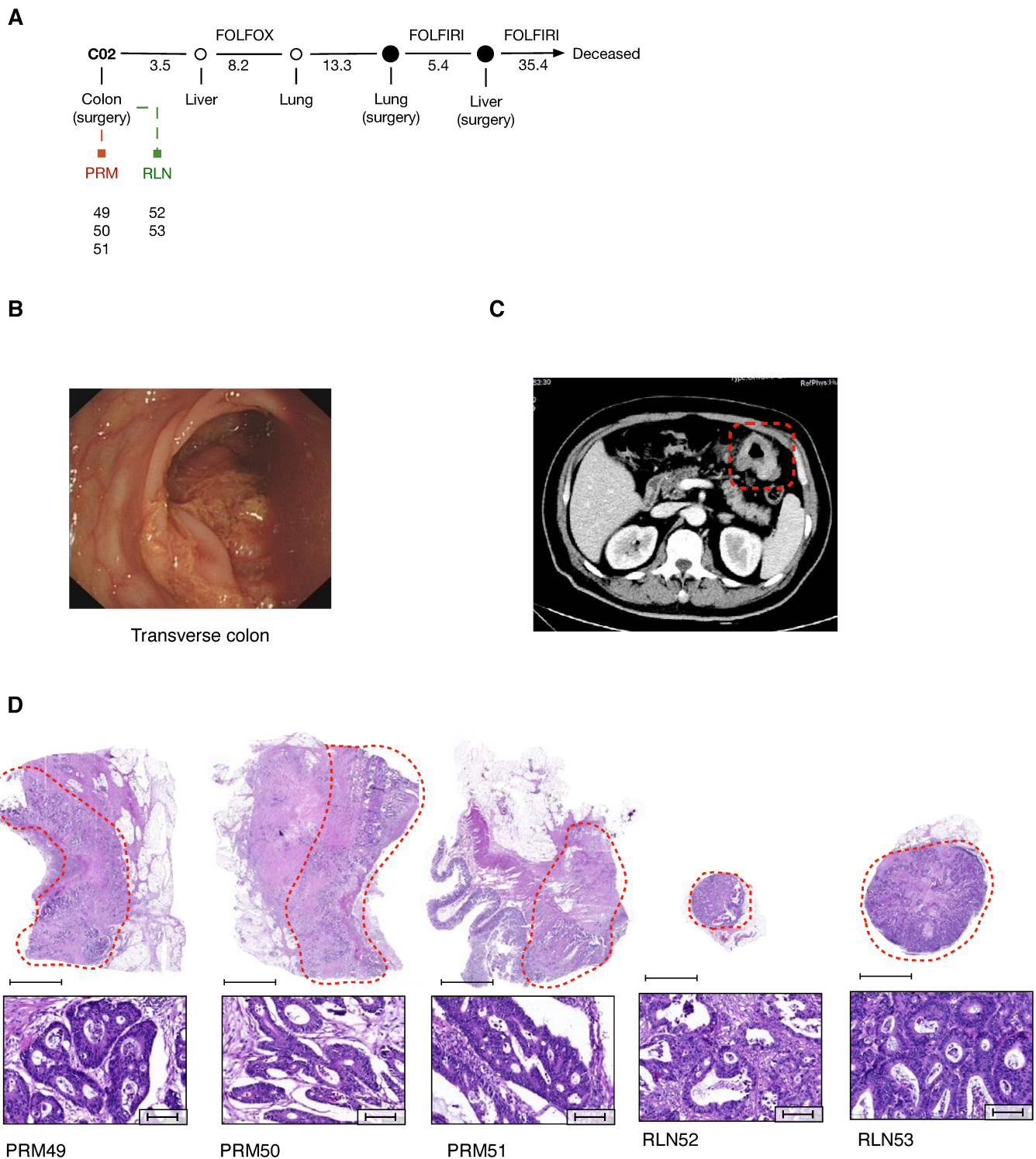


C



Data S1-4. Pathological H&E evaluation of secondary LUM in patient C01

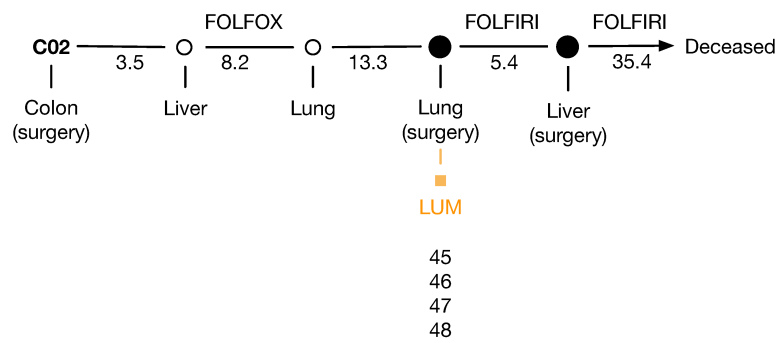
(A) Surgical time point of tumor resection; (B) CT imaging of lung metastasis. The same anatomical level of CT/MRI slice of metastatic event was demonstrated in rows across time points (months); (C) LUM31 was selected from the 1.7 cm × 1 cm × 0.6 lung metastasis. TLN33 to TLN35 were taken from lung lymph node. TLN33, TLN34 and TLN35 were taken from lymph node with 3.5 cm, 1 cm and 2.2 cm in diameter, respectively. Tumorous region is marked by dashed red line; Scale bar for microscopic images, 100 μm; Scale bar for gross images, 5 mm



Data S1-5. Pathological H&E evaluation of PRM and RLN in patient C02

(A) Surgical time point of tumor resection; (B) Preoperative images taken by colonoscopy; (C) CT imaging of primary tumor. (D) A 4.5 cm x 3.5 cm x 2 cm ulcerative tumor mass was resected surgically. PRM49 to PRM51 were taken from the tumor with peripheral colonic tissue. RLN52 was taken from a transverse mesenteric lymph node with 1cm in diameter, while RLN53 was taken from a paraneoplastic lymph node with 1.5 cm in diameter. Tumorous region is marked by dashed red line; Scale bar for microscopic images, 100 μ m; Scale bar for gross images, 5 mm.

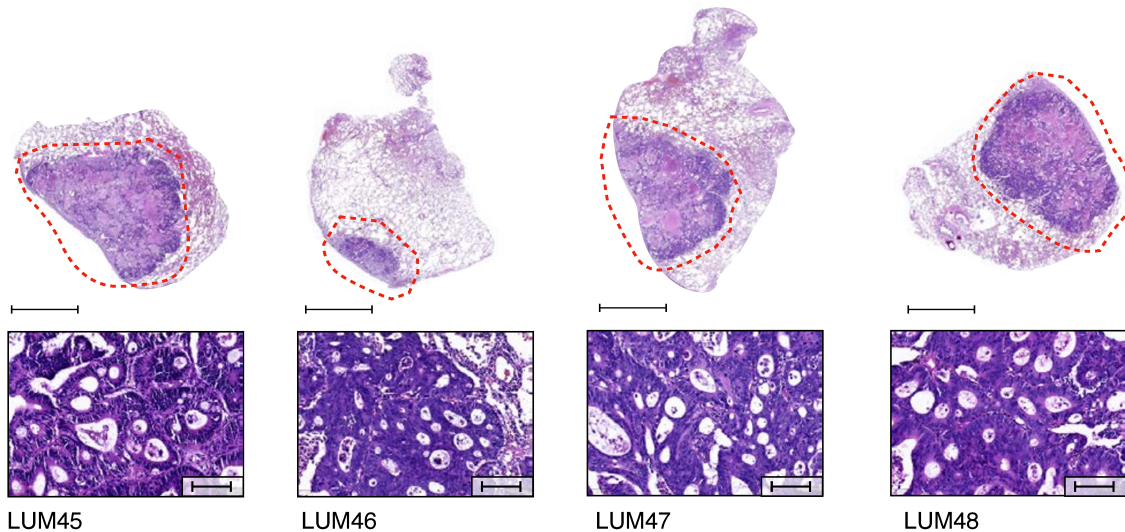
A



B



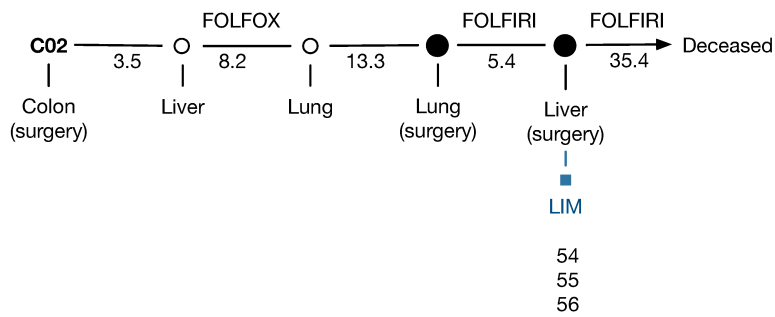
C



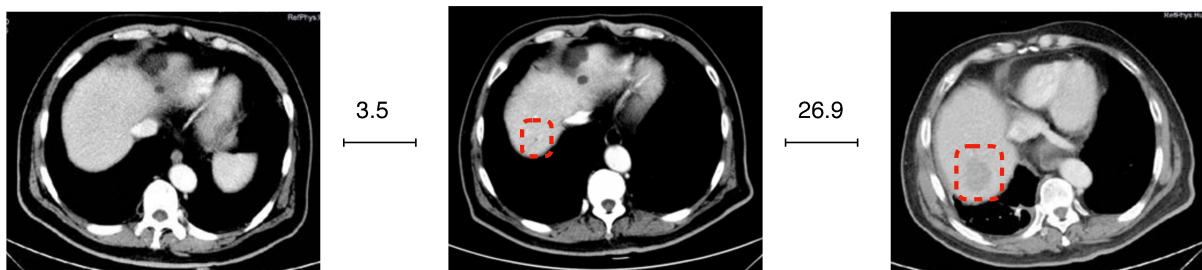
Data S1-6. Pathological H&E evaluation of LUM in patient C02

(A) Surgical time point of tumor resection; (B) CT imaging of lung metastasis. The same anatomical level of CT/MRI slice of metastatic event was demonstrated in rows across time points (months); (C) LUM45 to LUM 48 were taken from a mass sized 1.5 cm × 1.2 cm × 1 cm with peripheral lung tissue. Tumorous region is marked by dashed red line; Scale bar for microscopic images, 100 μm; Scale bar for gross images, 5 mm

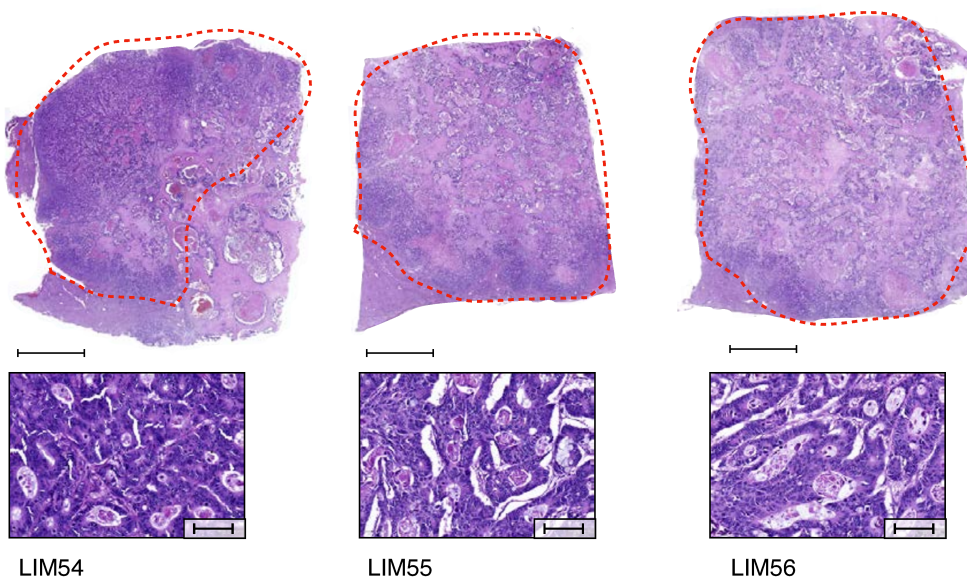
A



B

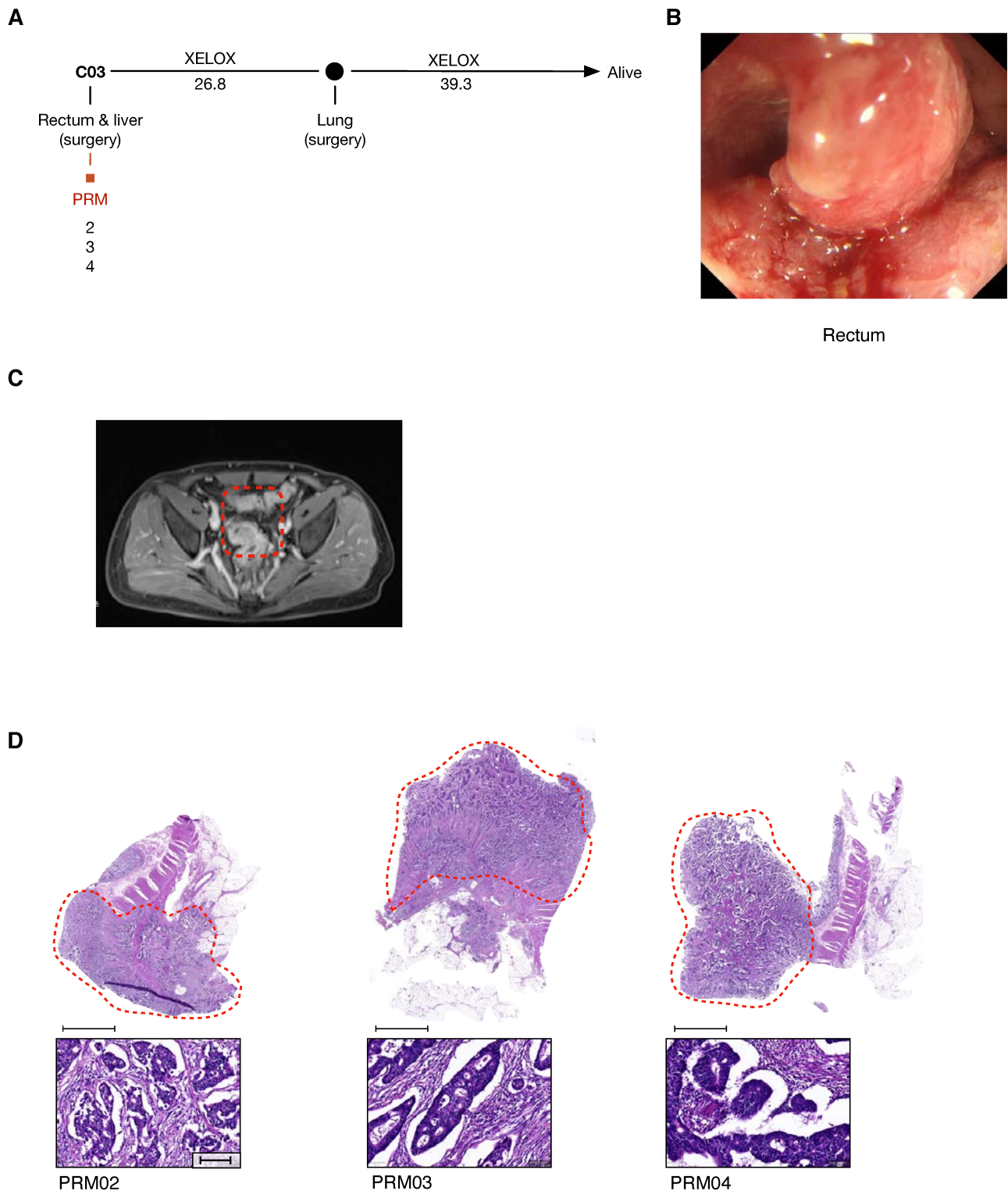


C



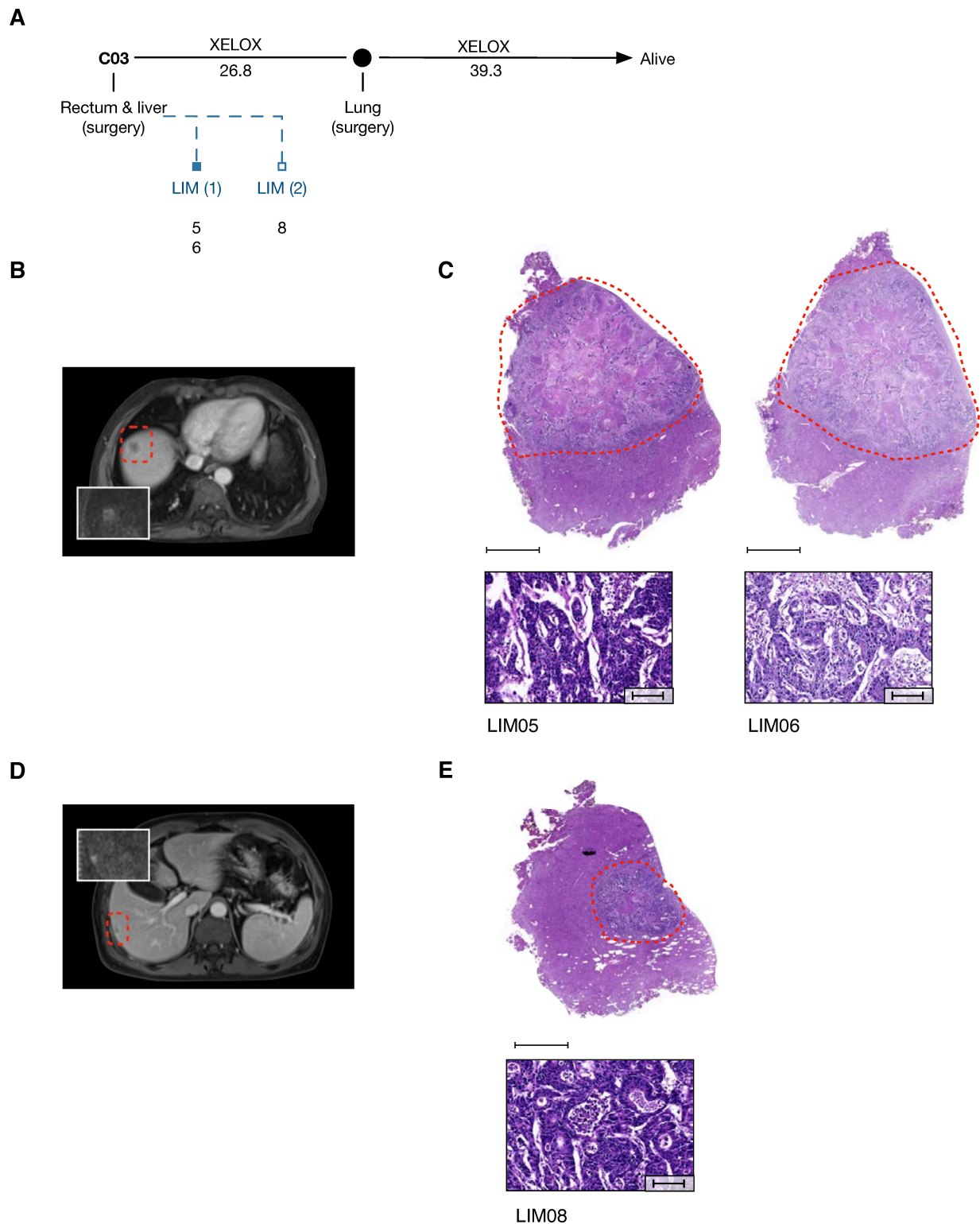
Data S1-7. Pathological H&E evaluation of LIM in patient C02

(A) Surgical time point of tumor resection; (B) CT imaging of liver metastasis in right lobe. The same anatomical level of CT/MRI slice of metastatic event was demonstrated in rows across time points (months); (C) A 4.0 cm x 3.0 cm x 2.0 cm metastatic tumor were removed. LIM54 to LIM56 were selected from the nodular mass with peripheral liver tissue or capsule. Tumorous region is marked by dashed red line; Scale bar for microscopic images, 100 μ m; Scale bar for gross images, 5 mm.



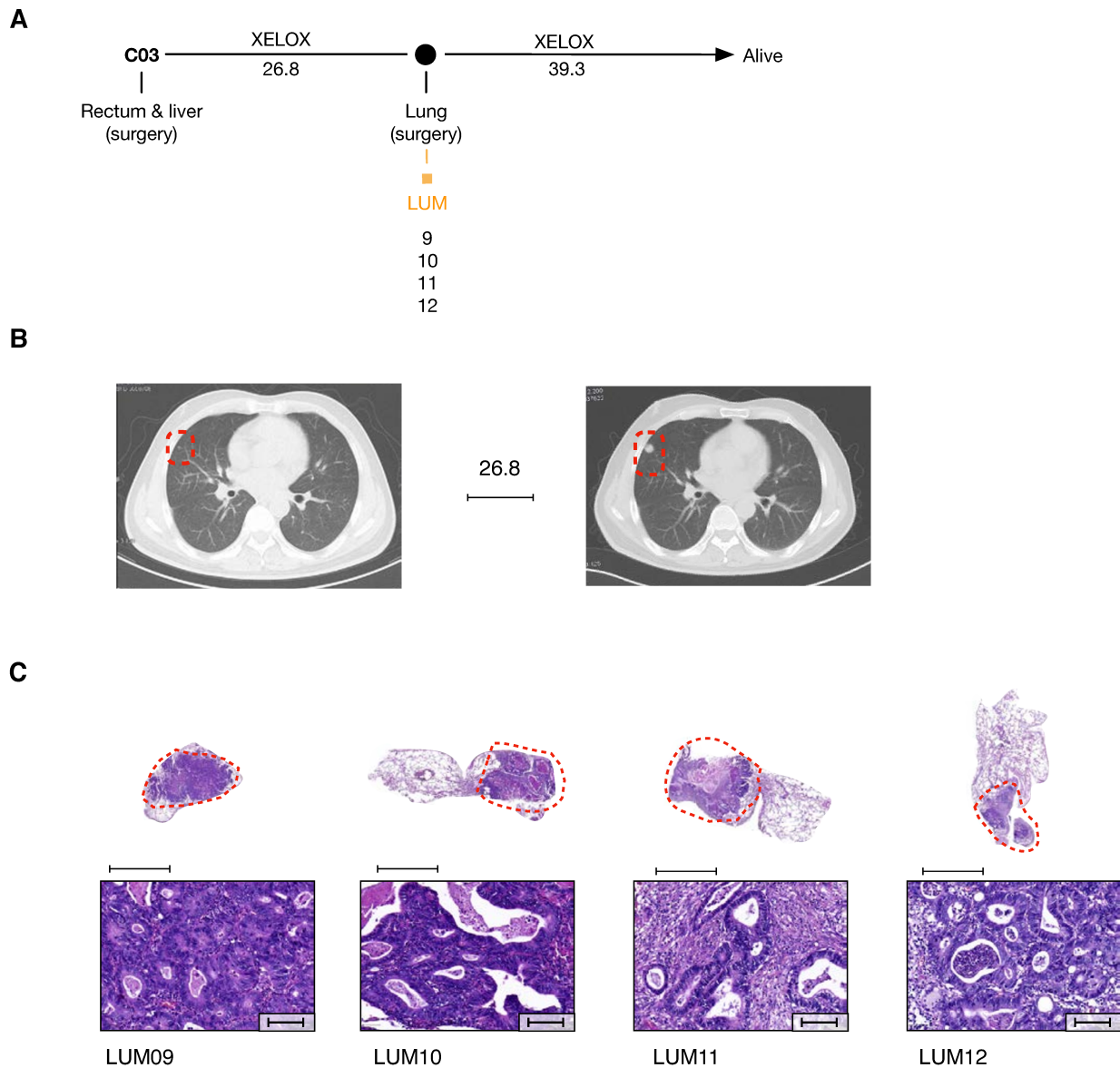
Data S1-8. Pathological H&E evaluation of PRM in patient C03

(A) Surgical time point of tumor resection; (B) Colonoscopic view of primary tumor in rectum; (C) MRI imaging of primary tumor; (D) A 4.5 cm × 3 cm × 1 cm nodular mass was resected. PRM02 to PRM04 were selected from the tumor with peripheral tissue. Tumorous region is marked by dashed red line; Scale bar for microscopic images, 100 μm; Scale bar for gross images, 5 mm.



Data S1-9. Pathological H&E evaluation of LIM in patient C03

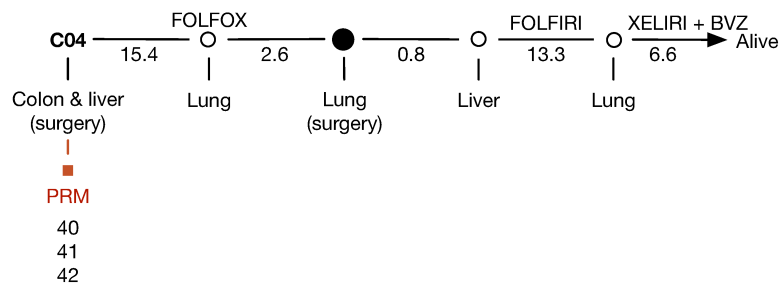
(A) Surgical time point of tumor resection; (B, D) MRI imaging of two liver metastases in right lobe at time of PRM diagnosis; (C) LIM05 and LIM06 were taken from the 3 cm × 2.5 cm × 2 cm liver metastatic nodule; (E) LIM08 was taken from another metastatic lesion with 2.5 cm × 1.5 cm × 1.5 cm in size. Tumorous region is marked by dashed red line; Scale bar for microscopic images, 100 μm; Scale bar for gross images, 5 mm.



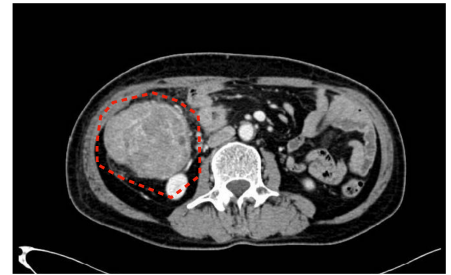
Data S1-10. Pathological H&E evaluation of LUM in patient C03

(A) Surgical time point of tumor resection; (B) CT imaging of lung metastasis in right lobe. The same anatomical level of CT/MRI slice of metastatic event was demonstrated in rows across time points (months); (C) A 1.5 cm × 1.2 cm × 1 cm metastatic nodule was resected. LUM09 to LUM12 were taken from the nodule with peripheral lung tissue. Tumorous region is marked by dashed red line; Scale bar for microscopic images, 100 μ m; Scale bar for gross images, 5 mm

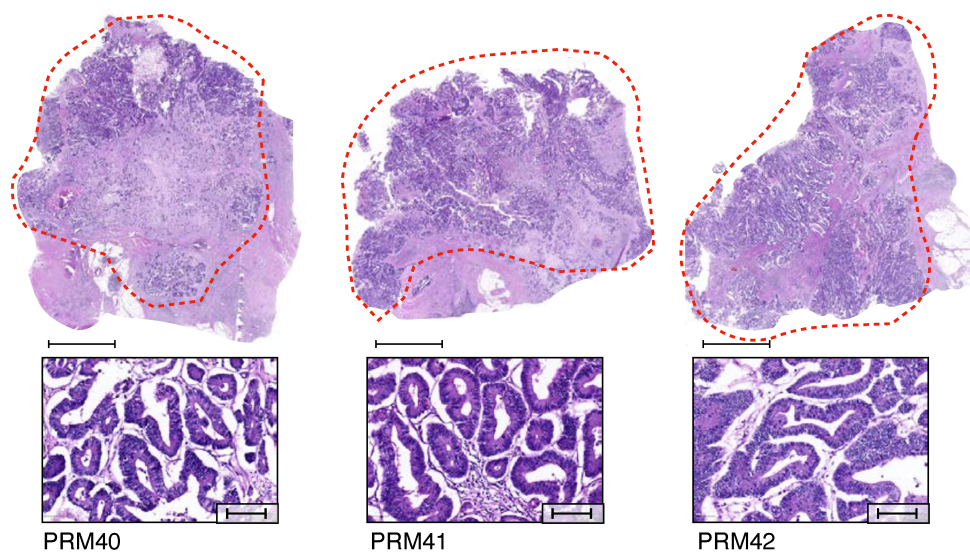
A



B



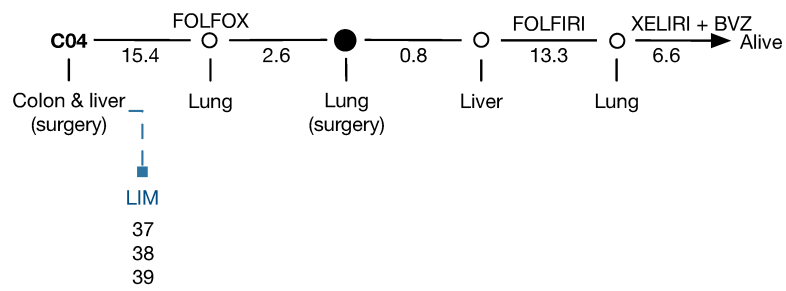
C



Data S1-11. Pathological H&E evaluation of PRM in patient C04

(A) Surgical time point of tumor resection; (B) CT imaging of primary colonic tumor; (C) A 5 cm x 7 cm x 4.5 cm mass was removed. PRM40 to PRM42 were taken from the mass. Tumorous region is marked by dashed red line; Scale bar for microscopic images, 100 μm; Scale bar for gross images, 5 mm.

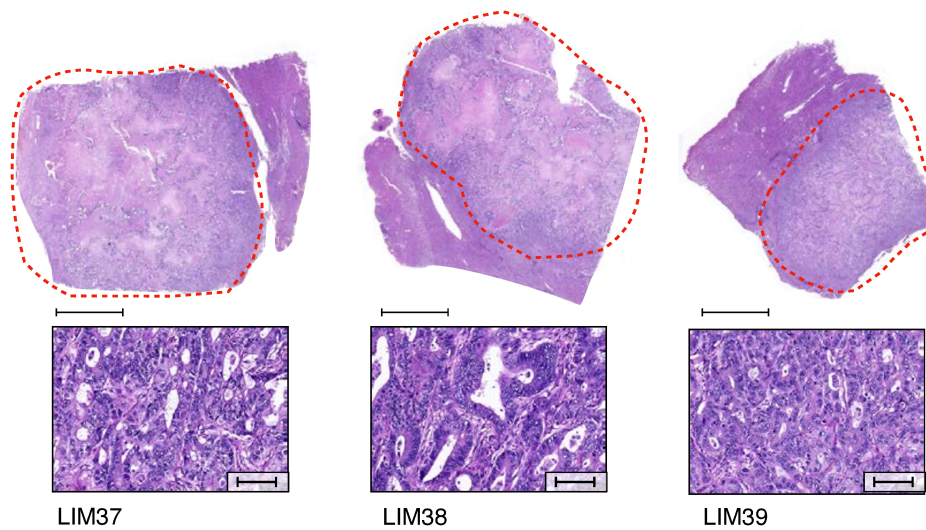
A



B

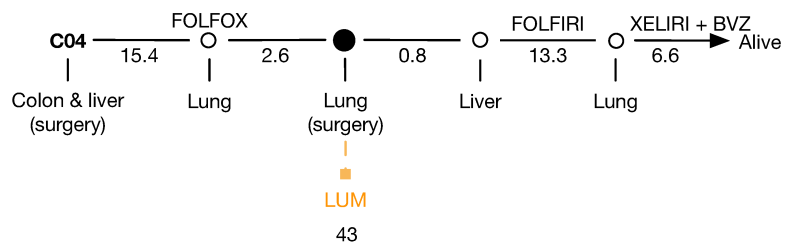
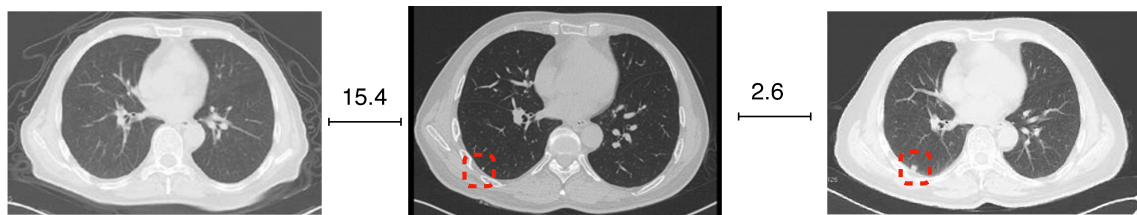
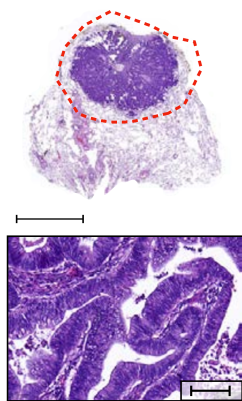


C



Data S1-12. Pathological H&E evaluation of LIM in patient C04

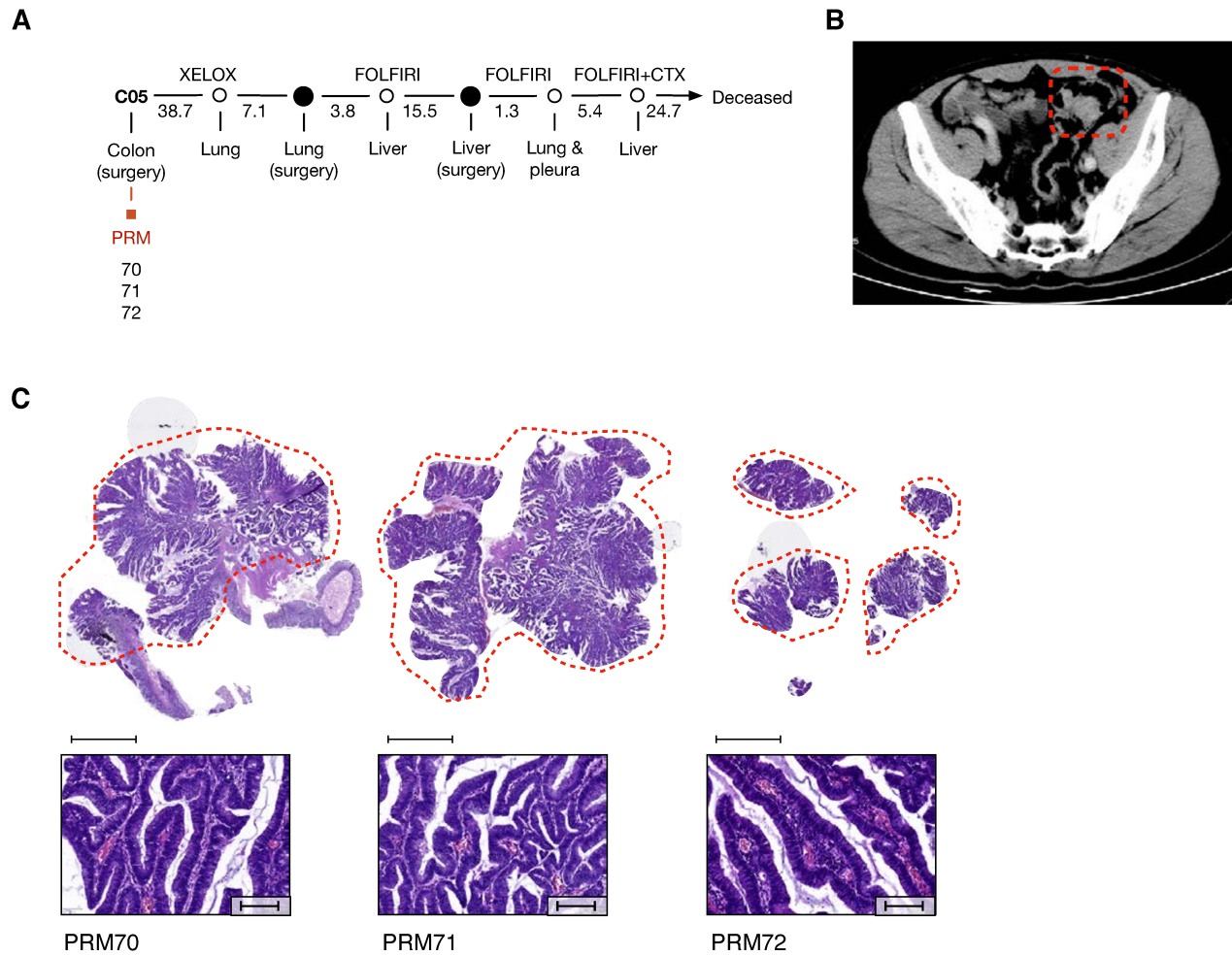
(A) Surgical time point of tumor resection; (B) CT imaging of liver metastasis in right lobe; (C) A nodular mass sized 2.5 cm x 2.2 cm x 1.8 cm was resected. LIM37 to LIM39 were taken from the tumor as well the surrounding liver tissue. Scale bar for microscopic images, 100 μ m; Scale bar for gross images, 5 mm

A**B****C**

LUM43

Data S1-13. Pathological H&E evaluation of LUM in patient C04

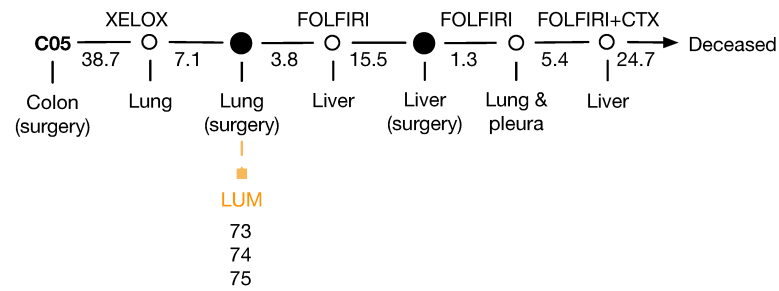
(A) Surgical time point of tumor resection; (B) CT imaging of lung metastasis in right lobe. The same anatomical level of CT/MRI slice of metastatic event was demonstrated in rows across time points (months); (C) A 0.8 cm × 0.8 cm × 0.5 cm nodule was removed. LUM43 was taken from the metastasis lesion with surrounding pleura. Scale bar for microscopic images, 100 μm; Scale bar for gross images, 5 mm.



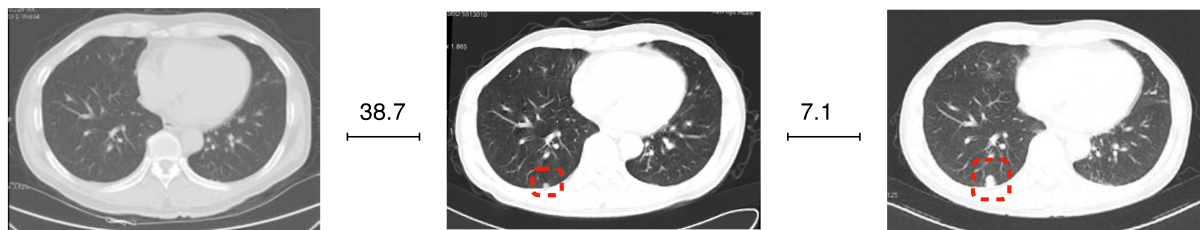
Data S1-14. Pathological H&E evaluation of PRM in patient C05

(A) Surgical time point of tumor resection; (B) CT imaging of primary tumor; (C) A 2.2 cm × 2 cm × 1.5 cm mass was resected. PRM70 to PRM72 were taken from tumor. Scale bar for microscopic images, 100 μm; Scale bar for gross images, 5 mm.

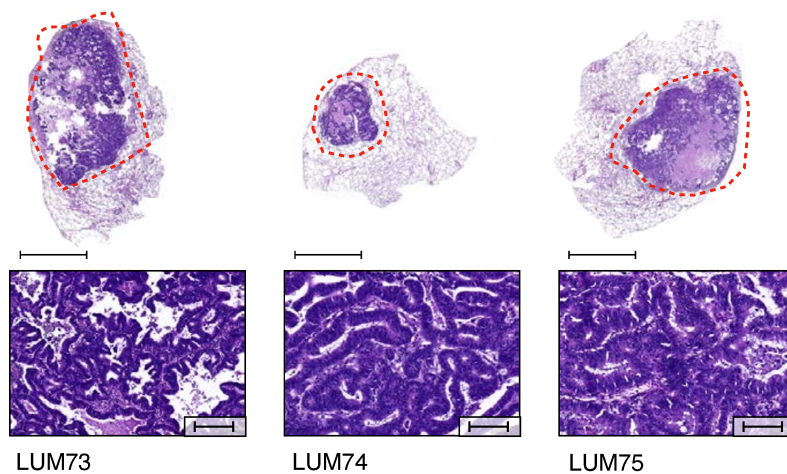
A



B



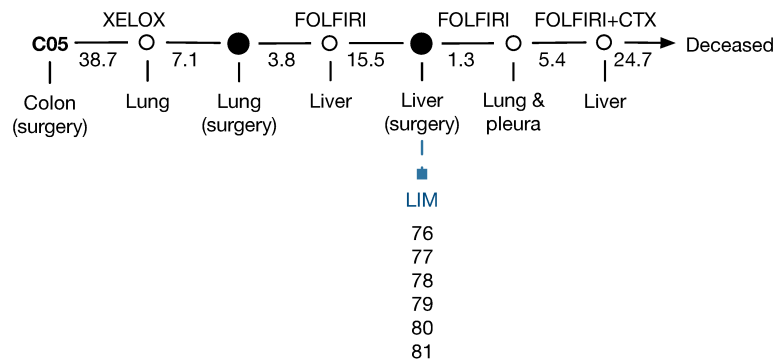
C



Data S1-15. Pathological H&E evaluation of LUM in patient C05

(A) Surgical time point of tumor resection; (B) CT imaging of lung metastasis in the right upper lobe. The same anatomical level of CT/MRI slice of metastatic event was demonstrated in rows across time points (months); (C) A 1.4 cm × 1 cm × 1.8 cm nodule was resected. LUM73 to LUM75 were taken from the nodule with surrounding lung tissue. Scale bar for microscopic images, 100 μm; Scale bar for gross images, 5 mm

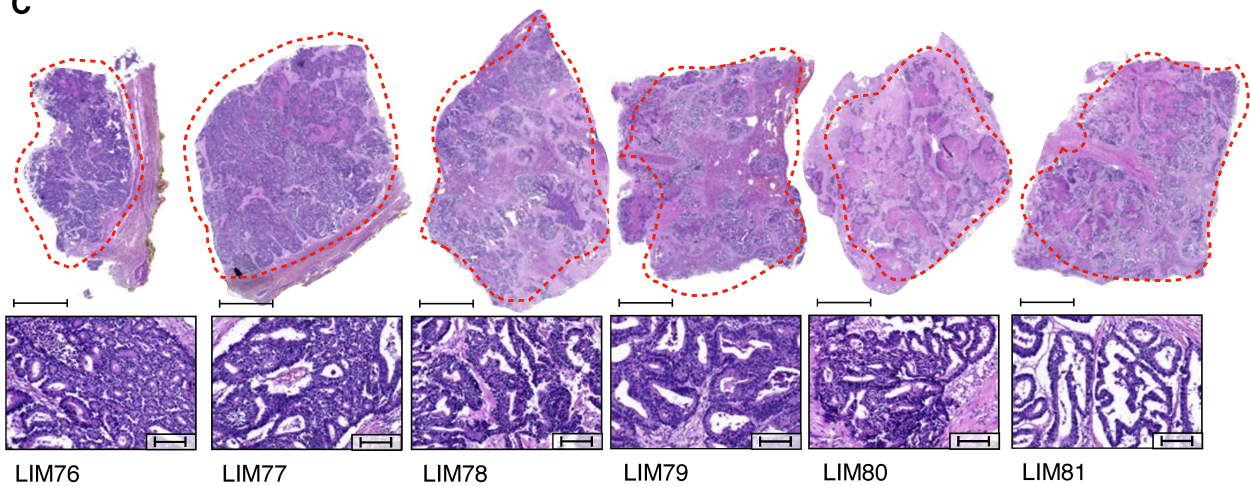
A



B

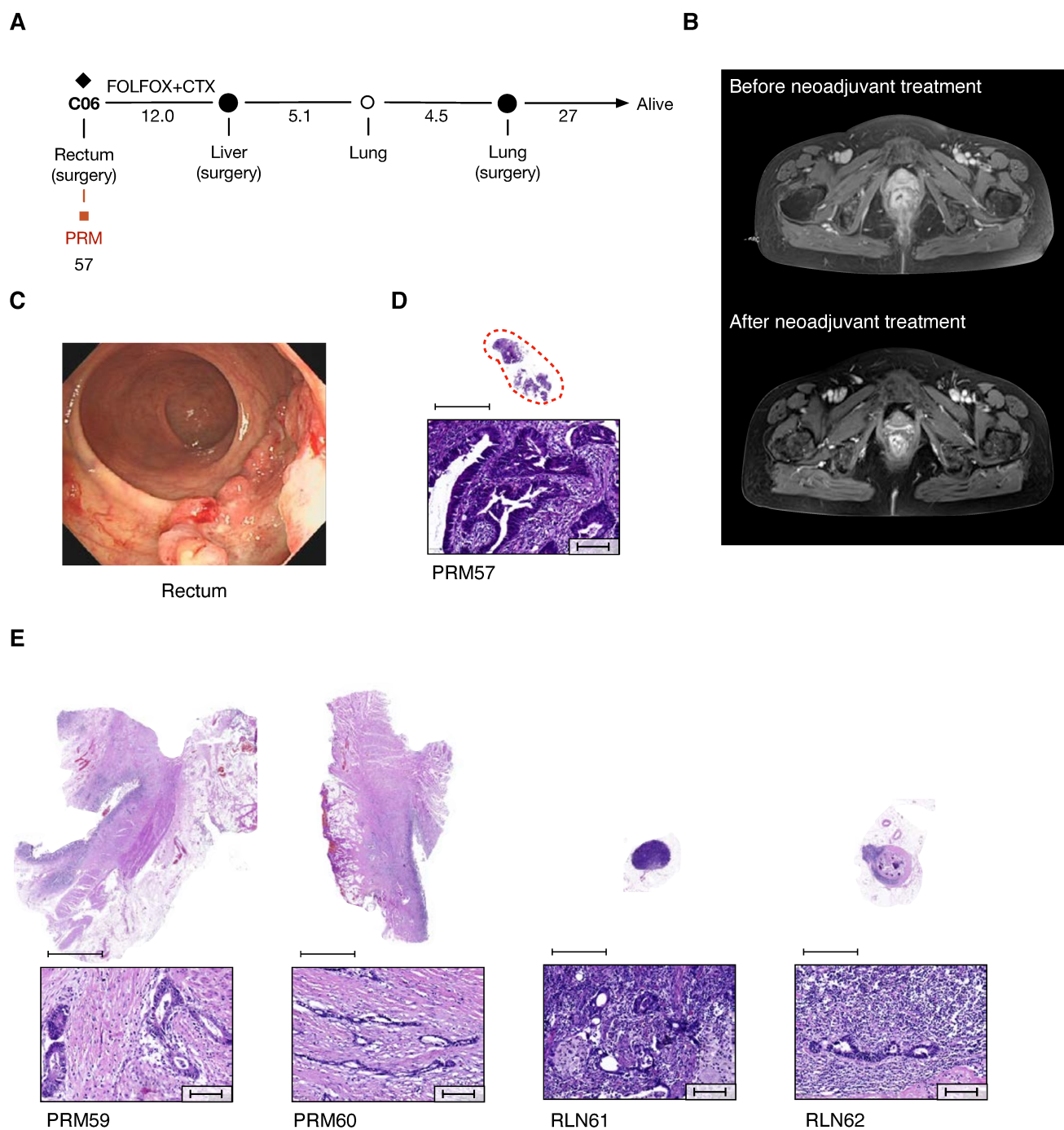


C



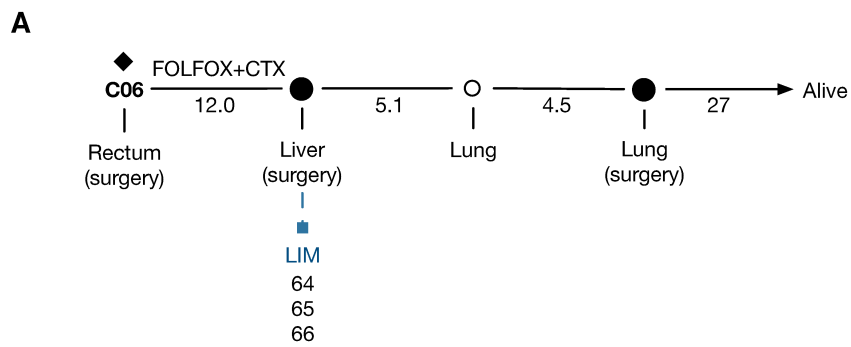
Data S1-16. Pathological H&E evaluation of LIM in patient C05

(A) Surgical time point of tumor resection; (B) CT imaging of liver metastasis in left lobe. The same anatomical level of CT/MRI slice of metastatic event was demonstrated in rows across time points (months); (C) A 19.3 cm x 13.2 cm x 6.8 cm mass was resected. LIM76 to LIM79 were taken from the mass with liver capsule. LIM80 and LIM81 were taken from the mass with peripheral liver tissue. Scale bar for microscopic images, 100 μ m; Scale bar for gross images, 5 mm.

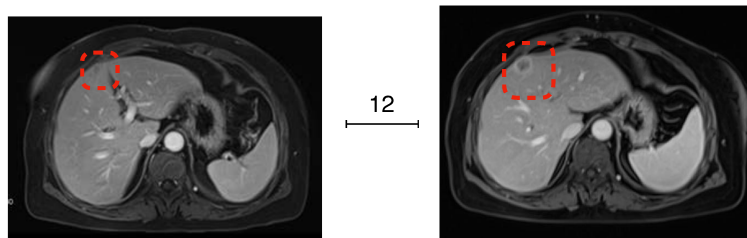


Data S1-17. Pathological H&E evaluation of PRM and RLN in patient C06

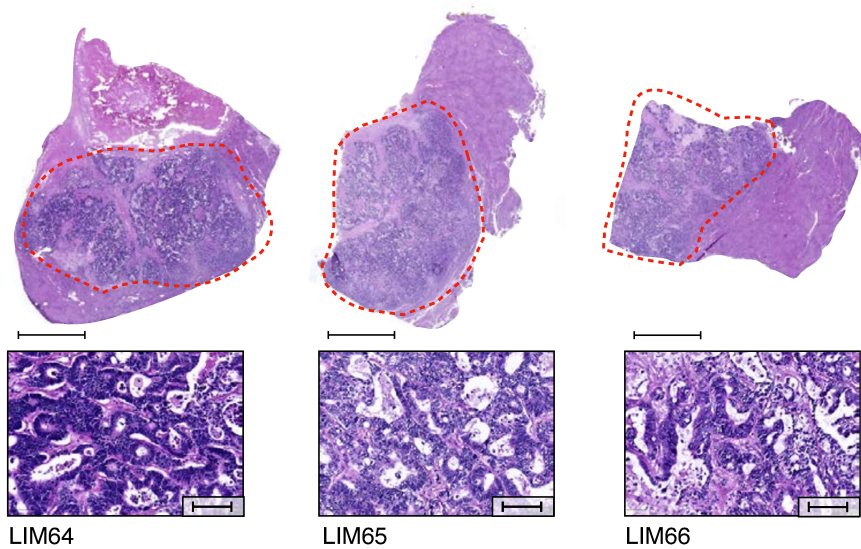
(A) Surgical time point of tumor resection; (B) MRI imaging of the primary tumor before and after neoadjuvant treatment; (C) Endoscopic picture of primary tumor at rectum before neoadjuvant treatment. (D) PRM57 was the biopsy during colonoscopy before neoadjuvant treatment; (E) A 3 cm × 2.3 cm × 0.4 cm mass after neoadjuvant treatment was resected. PRM59 and PRM60 were taken from the tumor with peripheral tissue. RLN61 and RLN62 were lymph nodes nearby tumor. These four samples have been excluded from phylogenetic analysis due to low tumor purity. Scale bar for microscopic images, 100 μm; Scale bar for gross images, 5 mm.



B



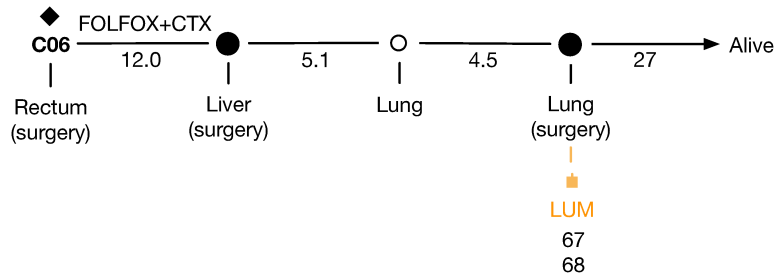
C



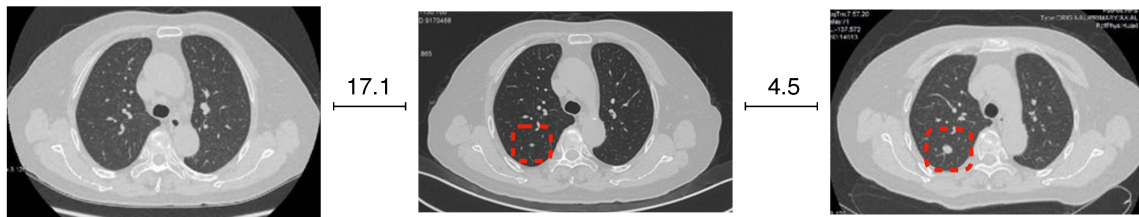
Data S1-18. Pathological H&E evaluation of LIM in patient C06

(A) Surgical time point of tumor resection; (B) MRI imaging of liver metastasis in left lobe. The same anatomical level of CT/MRI slice of metastatic event was demonstrated in rows across time points (months); (C) A 3 cm × 2 cm × 2 cm nodule was resected. LIM64 to LIM66 were taken from the nodule with surrounding liver tissue. Scale bar for microscopic images, 100 μm; Scale bar for gross images, 5 mm.

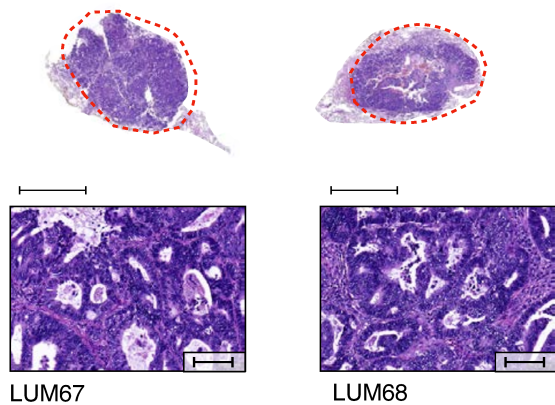
A



B



C



Data S1-19. Pathological H&E evaluation of LUM in patient C06

(A) Surgical time point of tumor resection; (B) CT imaging of lung metastasis in right upper lobe. The same anatomical level of CT/MRI slice of metastatic event was demonstrated in rows across time points (months); (C) A 2.6 cm \times 1.4 cm \times 1.1 cm nodule was resected. LUM67 and LUM68 were taken from the tumor with surrounding lung tissue. Scale bar for microscopic images, 100 μ m; Scale bar for gross images, 5 mm.