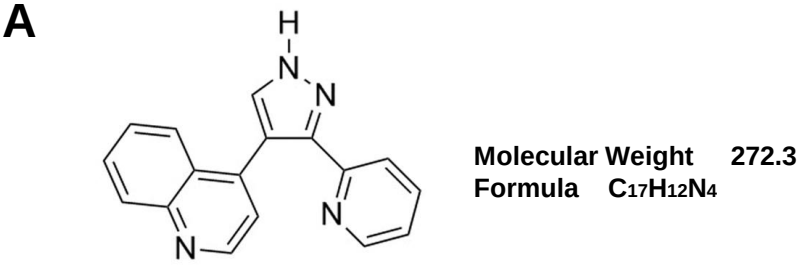
# Suppl. Fig S1


A
H
N
N
N
N
Molecular Weight 272.3
Formula C17H12N4
B
Total collagen (µg/mg)
**
*
Vehicle
TβRi 2d
TβRi 7d
C
Concentration (ng/mg)
NS
NS
NS
Vehicle
TβRi
Gem
TβRi+Gem
dFdC
dFdU
dFdCTP
D
Total CAFs
myCAFs
iCAFs
% podoplanin of total alive cells
% SAM+ of podoplanin+ cells
% Ly6C+ of podoplanin+ cells
NS
Vehicle
TβRi 14d
E
Total CAFs
myCAFs
iCAFs
% podoplanin+ of total alive cells
% SMA+ of podoplanin+ cells
% Ly6C+ of podoplanin+ cells
Vehicle
TβRi 2d
TβRi 4w
F
α-pSMAD2 / α-SMA
DAPI / α-SMA
100µm
100µm
% pSMAD2+SMA+/ SMA+ cells
***
*
Vehicle
TβRi 2d
TβRi 7d

**Supplemental Figure S1**. CAF populations adapt to prolonged TβR-I inhibitor-induced stromal modulation. **A**. Chemical structure of LY364947. **B**. Total collagen content (µg/mg tissue) in KP16 tumor lysates (after alkaline hydrolysis and measurement of hydroxyproline). **C**. Intratumoral gemcitabine levels after 14 days treatment of KP16 animals, N=8 mice per group. Mice were treated with vehicle or TβR-I inhibitor every other day, gemcitabine twice weekly, or the combination for 14 days. All groups received one dose of gemcitabine before tumor harvest. dFdC, 2'-deoxy-2',2'-difluorocytidine; dFdU, 2',2'-difluorodeoxyuridine; dFdCTP, 2',2'-difluorodeoxycytidine-5'-triphosphate. **D**. CAF populations return to baseline upon extended TβR-I antagonism in KP16 tumors. Quantification of CAF populations by flow cytometry treated for 14 days with vehicle and TβR-I inhibitor. **E**. Quantification of flow cytometry analysis of KPC tumor digests treated with vehicle and TβR-I inhibitor for 2 days (top) or 4 weeks (bottom) of CAF populations.

**F**. SMA+ CAFs develop resistance to TβR-I inhibitor-induced suppression of SMAD2 upon prolonged treatment. Left, representative confocal microscopy images of KP16 tumors co-stained with α-phospho-SMAD2 (red) and SMA (green), addition of DAPI (blue) filters red signal. Quantification of pSMAD2+ SMA+ versus total SMA+ cells by HALO Image Analysis after images were acquired by Aperio FL Multi-channel Fluroscence Slide Scanner, N≥4 tumors per group. Scale bars, 100 µm.