Supplemental

Figure S1 Hematologic profile (white blood cell count (WBC), hematocrit (HCT), and platelet count) of 3 patients receiving combination therapy starting at cycle 7 (indicated by dotted line). Patient responses after combination therapy were CR, PR and NR from top to bottom.

Figure S2 Photomicrographs of bone marrow histopathologic features at baseline and at time of response assessment with idasanutlin treatment alone (subjects 1, 2 and 5) or in combination with Pegasys (Subjects 3 and 4).

Subject 1 (Row A, first time-point; Row B, second time-point), showing normalization of bone marrow cellularity from 65% to 50% (A1, B1), with normalization of megakaryocyte number and morphology (A2, B2). Neither specimen showed evidence of fibrosis (MF0) (A3, A4, B3, B4).

Subject 2 (Row C, first time-point; Row D, second time-point), showing reduction of bone marrow cellularity from 60% to 50% (C1, D1), with normalization of megakaryocyte number and morphology (C2, D2). Both specimens showed mild fibrosis (MF1) (C3, C4, D3, D4).

Subject 3 (Row E, first time point; Row F, second time point), showing increase of bone marrow cellularity from 70% to 90% (E1, F1), without significant change in megakaryocyte number or morphology (E2, F2). Both specimens showed mild fibrosis (MF1) (E3, E4, F3, F4).

Subject 4 (Row G, first time point; Row H, second time point, showing decrease in fibrosis from MF2 (G3, G4), to MF1 (H3, H4). Otherwise the histological features were similar, with cellularity of 100% (G1), subsequently 95-100% (G2), and similar megakaryocytic number and morphology (G2, H2).

Subject 5 (Row I, first time-point; Row J, second time-point), showing reduction of bone marrow cellularity from 65% to 50% (I1, J1), with no significant change in megakaryocyte number or morphology (I2, J2), between the time points. Neither of these specimens showed evidence of fibrosis (MF0) (I3, I4, J3, J4).

Figure S1

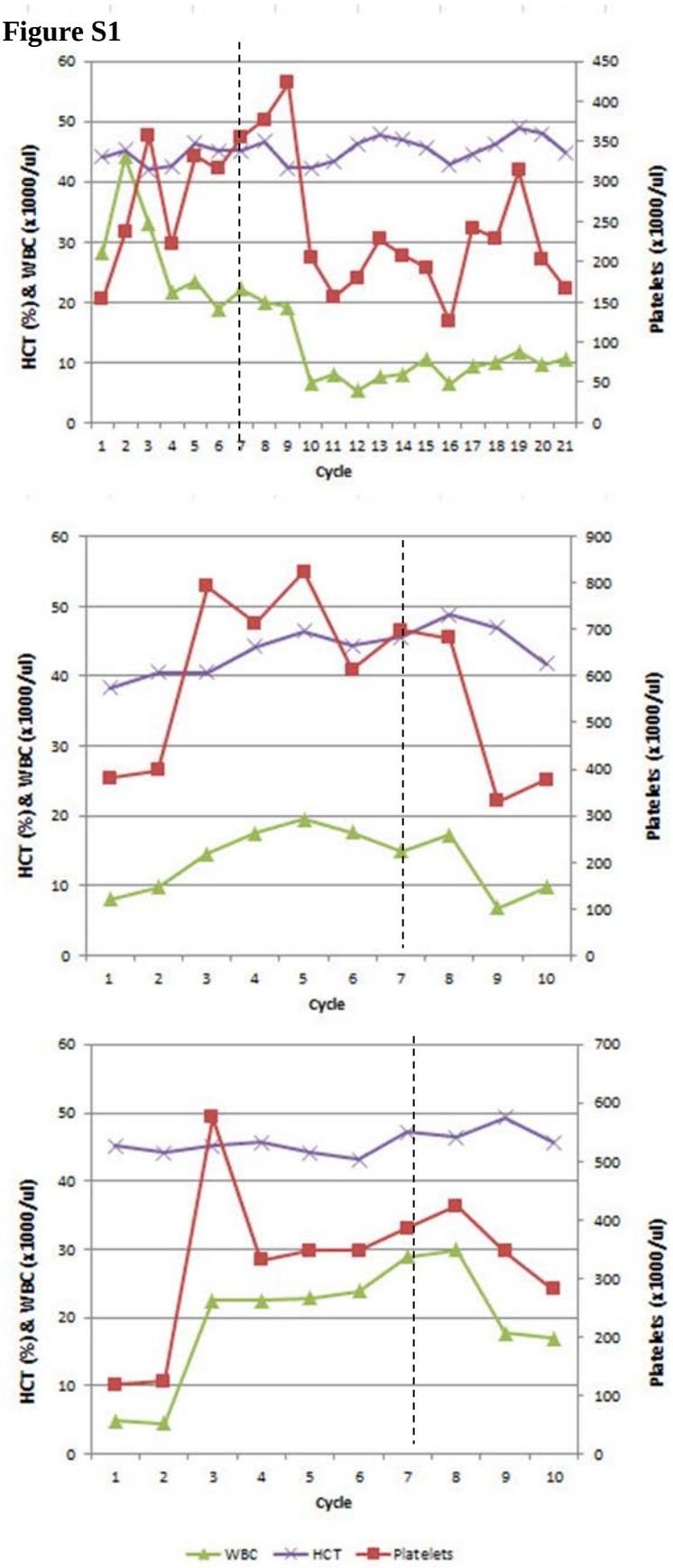
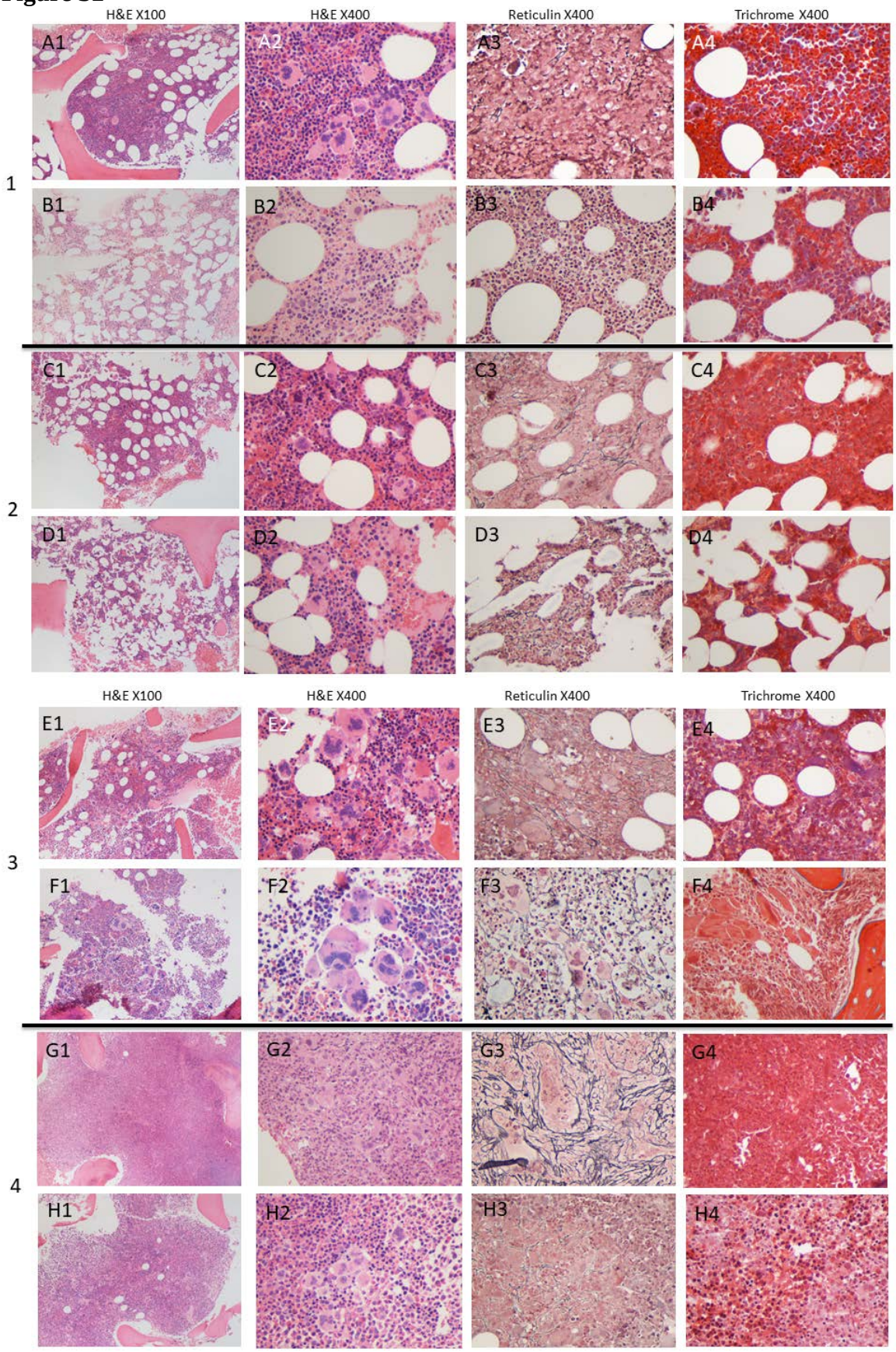


Figure S2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H&E X400
Reticulin X400
Trichrome X400
1
2
3
4
A1
A2
A3
A4
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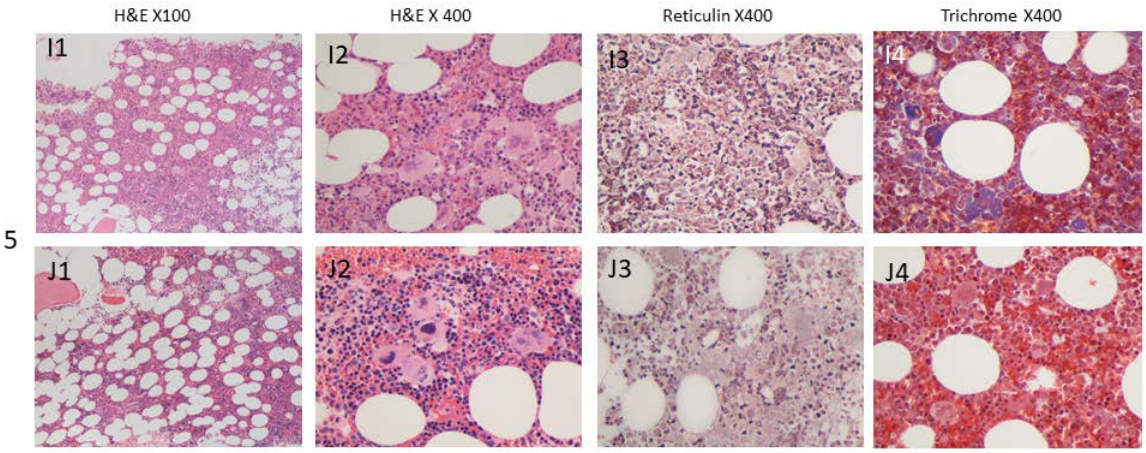
B2
B3
B4
C1
C2
C3
C4
D1
D2
D3
D4
E1
E2
E3
E4
F1
F2
F3
F4
G1
G2
G3
G4
H1
H2
H3
H4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H&E X 400
Reticulin X400
Trichrome X400
I1
I2
I3
I4
J1
J2
J3
J4