**Supplementary Table S1:** Summary of Actions Taken with Pexidartinib as a Result of Adverse Events at Least Possibly Related to Pexidartinib

| Number of Patients: | 600 mg (N=9) | 800 mg (N=3) | 1000 mg (N=3) | 1200 mg (N=6) | 1600 mg (N=33) | All Cohorts (N=54) |
|---|---|---|---|---|---|---|
| Pexidartinib Temporarily Withdrawn | 2 | 0 | 2 | 3 | 12 | 19 |
| Pexidartinib Dose Reduced | 0 | 0 | 0 | 2 | 4 | 6 |
| Pexidartinib Permanently Withdrawn | 1 | 0 | 0 | 0 | 4 | 5 |

**Supplementary Table S2:** Summary of Actions Taken with Paclitaxel as a Result of Adverse Events at Least Possibly Related to Paclitaxel

| Number of Patients: | 600 mg (N=9) | 800 mg (N=3) | 1000 mg (N=3) | 1200 mg (N=6) | 1600 mg (N=33) | All Cohorts (N=54) |
|---|---|---|---|---|---|---|
| Paclitaxel Temporarily Withdrawn | 2 | 0 | 2 | 3 | 14 | 21 |
| Paclitaxel Dose Reduced | 1 | 0 | 1 | 1 | 4 | 7 |
| Paclitaxel Permanently Withdrawn | 0 | 0 | 0 | 0 | 4 | 4 |

**Supplementary Table S3: Adverse Events by Dose Level and Severity Grade**

| Adverse Event Severity Grade | 600 mg (n=9) n (%) | 800 mg (n=3) n (%) | 1000 mg (n=3) n (%) | 1200 mg (n=6) n (%) | 1600 mg (n=33) n (%) | Total (N=54) n (%) |
|---|---|---|---|---|---|---|
| Any Event | 9 (100) | 3 (100) | 3 (100) | 6 (100) | 33 (100) | 54 (100) |
| Grade 1 (Mild) | 1 (11) | 0 | 0 | 0 | 1 (3) | 2 (4) |
| Grade 2 (Moderate) | 3 (33) | 1 (33) | 0 | 2 (33) | 1 (3) | 7 (13) |
| Grade 3 (Severe) | 4 (44) | 1 (33) | 1 (33) | 4 (67) | 27 (82) | 37 (69) |
| Grade 4 (Life Threatening) | 1 (11) | 1 (33) | 1 (33) | 0 | 4 (12) | 7 (13) |
| Grade 5 (Fatal) | 0 | 0 | 1 (33) | 0 | 0 | 1 (2) |

**Supplementary Table S4: Adverse Events by Dose Level Relationship to Study Drug**

| | 600 mg (n=9) n (%) | 800 mg (n=3) n (%) | 1000 mg (n=3) n (%) | 1200 mg (n=6) n (%) | 1600 mg (n=33) n (%) | Total (N=54) n (%) |
|---|---|---|---|---|---|---|
| **By Relationship to Paclitaxel** | | | | | | |
| **Any Event** | 9(100) | 3(100) | 3(100) | 6(100) | 33(100) | 54(100) |
| **Not Related** | 1 (11) | 0 | 0 | 0 | 2 (6) | 3 (6) |
| **Possibly Related** | 3 (33) | 0 | 0 | 1 (17) | 9 (27) | 13 (24) |
| **Probably Related** | 5 (56) | 3(100) | 3(100) | 5 (83) | 22 (67) | 38 (70) |
| **By Relationship to Pexidartinib** | | | | | | |
| **Any Event** | 9(100) | 3(100) | 3(100) | 6(100) | 33(100) | 54(100) |
| **Not Related** | 1 (11) | 0 | 0 | 0 | 2 (6) | 3 (6) |
| **Possibly Related** | 5 (56) | 0 | 0 | 1 (17) | 11 (33) | 17 (31) |

**Supplementary Table S5:** Summary of toxicities that occurred in >10% of patients and were at least possibly related to Pexidartinib:

| Toxicity | Grades 1 & 2 | Grades 3 & 4 | All Grades |
|---|---|---|---|
| | Number (%) | | |
| Fatigue | 24 (44) | 8 (15) | 32 (59) |
| Aspartate Aminotransferase Increased | 15 (28) | 4 (7) | 19 (35) |
| Nausea | 16 (30) | 3 (6) | 19 (35) |
| Anaemia | 10 (19) | 8 (15) | 18 (33) |
| Blood Creatine Phosphokinase Increased | 17 (31) | 0 (0) | 17 (31) |
| White Blood Cell Count Decreased | 15 (28) | 1 (2) | 16 (30) |
| Diarrhoea | 14 (26) | 2 (4) | 16 (30) |
| Decreased Appetite | 16 (30) | 0 (0) | 16 (30) |
| Neutropenia/Decreased Neutrophils | 9 (17) | 5 (9) | 14 (26) |
| Vomiting | 12 (22) | 2 (4) | 14 (26) |
| Dysgeusia | 14 (26) | 0 (0) | 14 (26) |
| Hypertension | 7 (13) | 6 (11) | 13 (24) |
| Rash | 8 (15) | 3 (6) | 11 (20) |
| Alanine Aminotransferase Increased | 9 (17) | 1 (2) | 10 (19) |
| Blood Alkaline Phosphatase Increased | 8 (15) | 1 (2) | 9 (17) |
| Hypophosphataemia | 3 (6) | 5 (9) | 8 (15) |
| Pruritus | 7 (13) | 0 (0) | 7 (13) |
| Periorbital Oedema | 7 (13) | 0 (0) | 7 (13) |
| Pyrexia | 6 (11) | 0 (0) | 6 (11) |
| Constipation | 6 (11) | 0 (0) | 6 (11) |

*Count includes only the maximum grade experienced by each patient for each AE term*

**Supplementary Table S6:** Summary of toxicities that occurred in >10% of patients and were at least possibly related to Paclitaxel

| Toxicity | Grades 1 & 2 | Grades 3 & 4 | All Grades |
|---|---|---|---|
| | Number (%) | | |
| Anaemia | 18 (33) | 14 (26) | 32 (59) |
| Fatigue | 25 (46) | 7 (13) | 32 (59) |
| Neutropenia/Decreased Neutrophils | 11 (20) | 12 (22) | 23 (43) |
| Diarrhoea | 16 (30) | 4 (7) | 20 (37) |
| Aspartate Aminotransferase Increased | 16 (30) | 3 (6) | 19 (35) |
| Lymphocyte Count Decreased | 8 (15) | 10 (19) | 18 (33) |
| White Blood Cell Count Decreased | 15 (28) | 2 (4) | 17 (31) |
| Nausea | 15 (28) | 2 (4) | 17 (31) |
| Decreased Appetite | 17 (31) | 0 (0) | 17 (31) |
| Dysgeusia | 15 (28) | 0 (0) | 15 (28) |
| Alopecia | 15 (28) | 0 (0) | 15 (28) |
| Vomiting | 12 (22) | 1 (2) | 13 (24) |
| Alanine Aminotransferase Increased | 9 (17) | 1 (2) | 10 (19) |
| Rash | 7 (13) | 2 (4) | 9 (17) |
| Neuropathy Peripheral | 6 (11) | 2 (4) | 8 (15) |
| Blood Alkaline Phosphatase Increased | 6 (11) | 1 (2) | 7 (13) |
| Pyrexia | 7 (13) | 0 (0) | 7 (13) |
| Hypophosphataemia | 3 (6) | 3 (6) | 6 (11) |
| Oedema Peripheral | 6 (11) | 0 (0) | 6 (11) |
| Pruritus | 6 (11) | 0 (0) | 6 (11) |

| | | | |
|---|---|---|---|
| Blood Creatine Phosphokinase Increased | 6 (11) | 0 (0) | 6 (11) |

*Count includes only the maximum grade experienced by each patient for each AE term*

**Supplemental Table 7:** Pexidartinib Day 15 Plasma Pharmacokinetic Parameters

| **Parameter** | **600 mg (n=6)** | **800 mg (n=3)** | **1000 mg (n=3)** | **1200 mg (n=6)** | **1600 mg (n=6)** |
|---|---|---|---|---|---|
| **$C_{max}$ (ng/mL) Mean (SD)** | 3655 (1447) | 6783 (1681) | 4443 (1165) | 8733 (3591) | 8772 (4055) |
| **$AUC^{0-4}$ (hr*ng/mL) Mean (SD)** | 13318 (5434) | 22290 (5242) | 13960 (5378) | 29495 (10391) | 28713 (1604) |