CLAIMS:

1. A method of treating a human for cancer comprising administering at least one dose of lapatinib, or a pharmaceutically acceptable salt or composition thereof, to a said human, wherein said human does not have one or more allelic polymorphisms selected from the group of: HLA-DQA1*0201, HLA-DQB1*0202, and/or HLA-DRB1*0701.

2. The method of claim 1, wherein said human is suffering from breast cancer.

3. The method according to claims 1 and 2, wherein said human is free of at least two polymorphisms selected from the group of: HLA-DRB1*0701, HLA-DQA1*0201, and/or HLA-DQB1*0202.

4. The method according to any one of claims 1 to 3 wherein said human is also free of the polymorphism in HLA-B*4403

5. The method according to any one of claims 1 to 4, wherein said human is also free of a polymorphism selected from rs12153855 and rs17207923 that reside in the gene TNXB.

6. The method according to any one of claims 1 to 5, wherein said human is also free of the Gilbert's syndrome variant UGT1A1*28.

7. The method according to any one of claims 1 to 6, wherein lapatinib, or a pharmaceutically acceptable salt or composition thereof, is administered to said human as monotherapy.

8. The method according to any one of claims 1 to 7 wherein said lapatinib, or a pharmaceutically acceptable salt or composition thereof, is co-administered with at least one other anti-cancer agent.

9. The method of claim 8, wherein said at least one other anti-cancer agent is selected from the group of: trastuzumab, capecitabine, paclitaxel, carboplatin, pazopanib and letrozole.

10. The method according to any one of claims 1 to 9 wherein said human shows a statistically significantly less hepatotoxicity when administered lapatinib, or a pharmaceutically acceptable salt or composition thereof, compared with a human having at least one polymorphism selected from the group of: HLA-DRB1*0701,

HLA-DQA1*0201, HLA-DQB1*0202 and HLA-B*4403 and/or a human having a genotype in TNXB, rs12153855 and/or rs17207923.

11. The method according to anyone of claims 1 to 10 wherein said human has both HLA-DQA1*0201 and HLA-DQB1*0202 polymorphisms.

12. The method according to anyone of claims 1 to 11 wherein said human is DQ2.2. seropositive.

13. The method according to any one of claims 1 to 12 wherein said human does not show significant elevation in alanine aminotransferase (ALT) and/or total bilirubin (TBL) after the administration of at least one dose of lapatinib, or a pharmaceutically acceptable salt or composition thereof.

14. A method of screening a human subject as an aid in predicting hepatotoxicity to lapatinib, or a pharmaceutically acceptable salt or composition thereof, administration, comprising determining whether the human has a HLA genotype associated with an increased risk of hepatotoxicity to lapatinib, or a pharmaceutically acceptable salt or composition thereof, compared to the risk expected in the general population, wherein the presence of such a HLA genotype indicates the human is at increased risk for a hepatotoxicity to lapatinib, or a pharmaceutically acceptable salt or composition thereof.

15. A method according to claim 14, further comprising treating said human subject with a therapeutic regime of lapatinib, or a pharmaceutically acceptable salt or composition thereof, when the human subject is not at increased risk of a hepatotoxicity to lapatinib, or a pharmaceutically acceptable salt or composition thereof.

16. A method according to claims 14 or 15, wherein the HLA genotype is selected from the group of: HLA-DQA1*0201, HLA-DQB1*0202, and HLA-DRB1*0701.

17. The method according to any one of claims 14 to 16 further comprising correlating the detection of an HLA-DQA1*0201, HLA-DQB1*0202, and/or HLA-DRB1*0701 allele with an increased risk of experiencing hepatotoxicity to lapatinib, or a pharmaceutically acceptable salt or composition thereof.

18. The method according to claims 14 to 17 further comprising determining if said subject has a genotype in HLA-B*4403 and/or TNXB, rs12153855 and/or rs17207923.

19. A method according to any one of claims 14 to 18 wherein said human is suffering from cancer.

20. The method according to any one of claims 14 to 19 wherein said human is suffering from breast cancer.

21. The method according to any one of claims 14 to 20 wherein said lapatinib, or a pharmaceutically acceptable salt or composition thereof, is administered as monotherapy.

22. The method according to any one of claims 14 to 21 wherein said lapatinib, or a pharmaceutically acceptable salt or composition thereof, is co-administered with at least one other anti-cancer agent.

23. The method according to anyone of claims 14 to 22 wherein said human has both HLA-DQA1*0201 and HLA-DQB1*0202 polymorphisms.

24. The method according to anyone of claims 14 to 23 wherein said human is DQ2.2. seropositive.

25. A method of treating a human subject in need of treatment with lapatinib, or a pharmaceutically acceptable salt or composition thereof, the method comprising:

(a) determining the genotype of the human subject at the HLA- DQA1, HLA-DQB1, HLA-DRB1, and/or HLA-B regions of chromosome 6; and

(b) administering lapatinib, or a pharmaceutically acceptable salt or composition thereof, to said human subject if polymorphic allele in an HLA gene is not detected.

26. The method according to claim 25 where said human is suffering from cancer.

27. The method according to claim 25 where said HLA gene is a MHC Class II HLA gene.

28. The method according to claim 27, wherein the polymorphic allele is selected from selected from the group of: HLA-DQA1*0201, HLA-DQB1*0202, and HLA-DRB1*0701.

29. The method of claim 28, wherein said human has at least one additional polymorphic allele.

30. The method according to claims 28 or 29, wherein said human has both HLA-DQA1*0201 and HLA-DQB1*0202 polymorphisms.

31. A method for prescribing lapatinib, or a pharmaceutically acceptable salt or composition thereof, to a human subject diagnosed with a medical condition suitable for treatment with lapatinib, or a pharmaceutically acceptable salt or composition thereof, comprising:

a. determining whether the human subject has at least one HLA genotype that has been associated with increased risk of hepatotoxicity, compared to the risk in the general population, and

b. where said human subject is not determined to have a genotype that has been associated with increased risk hepatotoxicity, prescribing treatment with lapatinib, or a pharmaceutically acceptable salt or composition thereof, to said human subject.

32. The method according to claim 31, wherein said HLA genotype that has been associated with an increased risk of hepatotoxicity is selected from the group of: HLA-DQA1*0201, HLA-DQB1*0202, and HLA-DRB1*0701.

33. The method according to claim 31 further comprising determining if the subject has a polymorphic genotype in TNXB selected from: rs12153855 and rs17207923.

34. The method according to claim 31 wherein said human subject has a polymorphic genotype in HLA-B*4403.

35. The method according to any one of claim 31 to 34 where said human subject has been diagnosed with cancer.

36. The method according to claim 35, wherein the cancer is breast cancer.

37. A method according to any one of claims 31 to 36 wherein said HLA genotype is determined by a method that detects the presence of the allelic DNA sequence.

38. A method of administering lapatinib, or a pharmaceutically acceptable salt or composition thereof, to reduce the incidence of hepatotoxicity, comprising:

    a. from a starting population of human subjects having a condition suitable for treatment with lapatinib, or a pharmaceutically acceptable salt or composition thereof, selecting a treatment population having a decreased percentage of subjects with an polymorphic allele in HLA compared to the starting population; and

    b. administering lapatinib, or a pharmaceutically acceptable salt or composition thereof, to said treatment population;

whereby the incidence of hepatotoxicity is reduced in the treatment population compared to the incidence of hepatotoxicity that would be expected to occur in the starting population.

39. A method of identifying a human subject at increased risk of experiencing a hypersensitivity reaction to a therapeutic regime of lapatinib, or a pharmaceutically acceptable salt or composition thereof, comprising:

    a. performing a genotyping technique on a biological sample from said subject to determine whether the human subject's HLA genotype includes an allele selected from HLA-DQA1*0201, HLA-DQB1*0202, or HLA-DRB1*0701;

    b. detecting an HLA-DQA1*0201, HLA-DQB1*0202, and/or HLA-DRB1*0701; and

    c. correlating the detection of an HLA-DQA1*0201, HLA-DQB1*0202, and/or HLA-DRB1*0701, allele with an increased risk of experiencing a hepatotoxicity to a therapeutic regime of lapatinib, or a pharmaceutically acceptable salt or composition thereof, compared to the risk if no HLA-DQA1*0201, HLA-DQB1*0202, and/or HLA-DRB1*0701, allele were detected.

40. The method according to claim 39 further comprising performing a genotyping technique on a biological sample from said human subject to determine whether the subject's has genotypes in TNXB rs12153855 and/or rs17207923 and correlating correlating the detection of an genotypes in TNXB rs12153855 and/or

rs17207923 with an increased risk of experiencing a hepatotoxicity to a therapeutic regime of lapatinib, or a pharmaceutically acceptable salt or composition thereof, compared to the risk if no genotypes in TNXB rs12153855 and/or rs17207923 were detected.

41. A method according to claim 39 or 40, wherein said biological sample is selected from the group consisting of cells, blood, blood components, urine and saliva.

42. The method according to claim 39 to 41, wherein said human is DQ2.2. seropositive.

43. The method according to anyone of claims 39 to 42 wherein said human is also free from (TA)7/(TA)7 genotype of UGT1A1.

44. A method of treating a human for cancer comprising administering at least one dose of lapatinib, or a pharmaceutically acceptable salt or composition thereof, to said human, wherein said human is genotyped as not having one or more allelic polymorphisms selected from the group of: HLA-DQA1*0201, HLA-DQB1*0202 and HLA-DRB1*0701.

45. A method of treating a human for cancer comprising administering at least one dose lapatinib, or a pharmaceutically acceptable salt or composition thereof, to said human, monitoring the level of ALT and/or bilirubin in said human's blood, genotyping said human for one or more allelic polymorphisms selected from the group of: HLA-DQA1*0201, HLA-DQB1*0202, and HLA-DRB1*0701, and/or genotypes in TNXB rs12153855 and/or rs17207923 if said human demonstrates an elevation in said ALT above 3xULN and/or said total bilirubin 2.0XULN.

46. The method of either of claims 44 or 45, further comprising administering at least a second dose of lapatinib to said human if said human does not have one or more allelic polymorphisms selected from the group of: HLA-DQA1*0201, HLA-DQB1*0202, and HLA-DRB1*0701.

47. The method of any one of claims 44 to 46 wherein said human is suffering from breast cancer.

48. The method of any one of claims 44 to 47 wherein said human is also free from (TA)7/(TA)7 genotype of UGT1A1.

49. A method of administering lapatinib, or a pharmaceutically acceptable salt or composition thereof, to a human comprising:
(a) administering at least a first dose of lapatinib, or pharmaceutically acceptable salt or composition thereof, to said human,
(b) monitoring at least one liver signal in said human,
(c) genotyping said human for one or more allelic polymorphisms selected from the group of: HLA-DQA1*0201, HLA-DQB1*0202, and HLA-DRB1*0701 if said liver signal becomes elevated after receiving at least one dose of lapatinib or pharmaceutically acceptable salt or composition thereof; and
(d) administering at least a second dose of lapatinib or pharmaceutically acceptable salt or composition thereof, to said human if the human does not have any of the polymorphisms of step (c).

50. The method of claim 49 wherein said liver signal is selected from ALT and TBL.

51. The method of either one of claims 49 or 50 wherein said human is suffering from breast cancer.

52. The method of any one of claims 49 to 51 wherein said ALT is elevated to above about 3.0XULN and/or TBL is elevated to above about 1.5XULN after at least one dose of lapatinib.

53. The method of any one of claims 49 to 52 wherein said human is also free polymorphisms and/or genotypes in TNXB rs12153855 and/or rs17207923.

54. The method of any one of claims 49 to 53 wherein said human is also free from (TA)7/(TA)7 genotype of UGT1A1.

55. The method according to anyone of claims 49 to 54 wherein said human has both HLA-DQA1*0201 and HLA-DQB1*0202 polymorphisms.

56. Use of lapatinib, or a pharmaceutically acceptable salt or composition thereof, for treating a human for cancer, wherein said human does not have one or more allelic polymorphisms selected from the group of: HLA-DQA1*0201, HLA-DQB1*0202, and/or HLA-DRB1*0701.

CLAIMS:

1. An invention not claimed in any divisional application.