An NCRI randomised study comparing dasatinib with imatinib in patients with newly diagnosed CML

# Acknowledgements

<table>
<thead>
<tr>
<th>Data analysis and presentation</th>
<th>Stephen O'Brien, Corinne Hedgley, Paul Terril, Philip Rowe, John McCullough</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial management and data collection, Newcastle</td>
<td>Corinne Hedgley, Lynn Seeley, Ruth Bescoby, Carrie Page, Angela Fallows, Laura Brown, Gemma Gills, Wendy Banks, Meg Buckley, Leanne Woolmer, Stephanie Clutterbuck, Wendy Osborne</td>
</tr>
<tr>
<td>PCR &amp; DNA/RNA biobanking</td>
<td>Letizia Foroni, Gareth Gerrard, Hammersmith</td>
</tr>
<tr>
<td>Cell biobanking</td>
<td>Tessa Holyoake, Alan Hair, Heather Jorgensen, Glasgow</td>
</tr>
<tr>
<td>Study Management Committee</td>
<td>SO'B, CH, Richard Clark, Liverpool; Jane Apperley, Hammersmith, Mhairi Copland (Chair of CML WG)</td>
</tr>
<tr>
<td>Data Monitoring Committee</td>
<td>John Goldman, Keith Wheatley, Graham Dark, Charles Schiffer</td>
</tr>
<tr>
<td>Sponsor</td>
<td>Newcastle Hospitals NHS Foundation Trust</td>
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<tr>
<td>Funder</td>
<td>Bristol-Myers Squibb: Glenn Kroog, Milayna Subar, Sonal Chavda-Sitaram</td>
</tr>
<tr>
<td>Chief Investigator</td>
<td>Stephen O'Brien</td>
</tr>
<tr>
<td>Sites</td>
<td>n=172. Thanks to all our investigators and site staff.</td>
</tr>
<tr>
<td>Patients</td>
<td>n=814. A huge thank you to all participating patients.</td>
</tr>
<tr>
<td>NCRI CML Working Group</td>
<td>Dragana Milojkovic, Jenny Byrne, Hugues de Lavallade, Adam Mead, Graeme Smith, Brian Huntly, Richard Szydlo, Andy Goringe, Naumann Butt, Sameer Tulpule, Shamyla Siddique, Bernie Ramsahoye, Mhairi Copland (Chair)</td>
</tr>
</tbody>
</table>
814 patients in total

Recruitment closed Feb 2013

172 hospitals set up, 145 recruited patients
Outline

Background
Design
What happened to all the patients?
Progressions and deaths
Adverse events
Cytogenetics & PCR
Summary
Outline

Background

Design

What happened to all the patients?

Progressions and deaths

Adverse events

Cytogenetics & PCR

Summary
• Imatinib still commonly used as first line therapy
• 2nd generation TKIs generally produce higher rates of major molecular response
• Dasision study* (n= 519) MR3 (MMR) at 3 years:
  • imatinib 55% (69% still on treatment)
  • dasatinib 69% (71% still on treatment)
• No difference in OS at 5 years
• Concerns about long term safety of 2nd gen
• SPIRIT 2 (n=814) is largest dasatinib trial

Kantarjian et al. NEJM (2010); 362:2260
Jabbour et al. Blood (2014); 123: 494-500
*rates are KM cumulative incidence
Cortes et al. Abstract 154, ASH 2014
TKIs in the UK

- Imatinib: Development → License → NICE approved (Off patent 2016)
- Dasatinib: Development → License → NICE approved
- Nilotinib: Development → License → NICE approved
- Bosutinib: Development → License → NICE approved
- Ponatinib: Development → License → NICE approved

Outline

Background

Design

What happened to all the patients?

Progressions and deaths

Adverse events

Cytogenetics & PCR

Summary
SPIRIT 2: study design

Chronic phase CML within 3 months of diagnosis

Arm A: Imatinib 400
n=814

Arm B: Dasatinib 100
N=407

Randomised, open label
Primary endpoint: 5 year EFS
Secondary: cytogenetic, PCR response, toxicity
Endpoints

Primary
• 5 year event free survival (EFS)
  – Assessed for all patients March 2018

Secondary
• Rate of complete cytogenetic response (CCR)
• Rate of Major Molecular Response
  – (MMR, MR$^3$, BCR-ABL1/ABL1 ratio<0.1%)
• Toxicity
• Treatment failure rates (TFR) after 5 years
• Rates of complete haematologic response (CHR)
• Overall survival at 2 and 5 years
Entry & exclusion criteria

**Entry**

1. Male or female patients ≥ 18 years of age.
2. Patients must have all of the following:
   i) be enrolled within 3 months of initial diagnosis of chronic phase CML
   ii) confirmation of the Philadelphia chromosome or variants of (9;22) translocations;
   iii) (a) < 15% blasts in peripheral blood and bone marrow;
    (b) < 30% blasts plus promyelocytes in peripheral blood and bone marrow;
     (c) < 20% basophils in peripheral blood,
     (d) ≥ 100 x 10^9/L platelets
   iv) no evidence of extramedullary leukaemic involvement, with the exception of hepatosplenomegaly.
3. Written voluntary informed consent.

**Exclusion**

1. Ph-negative, BCR-ABL1-positive, disease not eligible
2. Any prior treatment for CML (hydroxycarbamide, anagrelide permitted)
3. Prior chemotherapy, including PBSC mobilisation
4. Prior autograft or allograft
5. ECOG Performance Status Score ≥ 3
6. >2x ULN liver, renal function; >1.5x ULN coag; warfarin OK
7. Uncontrolled medical disease; known HIV pos; major surgery within 4 weeks
8. Patients who are: pregnant; breast feeding; not on appropriate contraception
9. Other malignancy within the past five years (except BCC)
Outline

Background
Design

What happened to all the patients?
Progressions and deaths
Adverse events
Cytogenetics & PCR

Summary
Patients enroled

Aug 2008 to Feb 2013
814 in 54 months: 15 per month

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Imatinib n=407 (%)</th>
<th>Dasatinib n=407 (%)</th>
<th>Total n=814 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>53.0</td>
<td>53.0</td>
<td>53.0</td>
</tr>
<tr>
<td>Range</td>
<td>18-87</td>
<td>18-89</td>
<td>18-89</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>165 (40.5)</td>
<td>156 (38.3)</td>
<td>321 (39.4)</td>
</tr>
<tr>
<td>Male</td>
<td>241 (59.2)</td>
<td>250 (61.4)</td>
<td>491 (60.3)</td>
</tr>
<tr>
<td>NK</td>
<td>1 (0.2)</td>
<td>1 (0.2)</td>
<td>2 (0.2)</td>
</tr>
<tr>
<td><strong>Available data for Sokal</strong></td>
<td><strong>SA2</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>242 (59.6)</td>
<td>246 (60.6)</td>
<td>488 (60.1)</td>
</tr>
<tr>
<td><strong>Follow up (months)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>36.9</td>
<td>38.3</td>
<td>37.4</td>
</tr>
<tr>
<td>Range</td>
<td>2 – 69</td>
<td>0 – 69</td>
<td>0 - 69</td>
</tr>
</tbody>
</table>
I'm not sure where these numbers came from originally? Do they need checking or as per BSH numbers is fine?

Sarah Adams, 8/15/2014
What happened to all the patients?

Randomised n=814

Allocated to imatinib – 407
  1 exclusion: Protocol violation
  Received imatinib – 406 (100%)

  Continued with imatinib – 236 (58.1)
    Follow up complete – 15 (3.7)
    Follow up on-going – 221 (54.4)

  Stopped imatinib – 170 (41.9)
    Death whilst on study drug – 7 (1.7)
    Decision to stop drug – 163 (40.1)

Status of 163 pts who stopped imatinib:
  - Subsequent death – 11 (2.7)
  - Follow up complete – 8 (2.0)
  - Follow up on-going – 124 (30.5)
  - Declined follow up – 13 (3.2)
  - Unknown – 7 (1.7)

Allocated to dasatinib – 407
  1 Exclusion: consent withdrawn
  Received dasatinib – 406 (100%)

  Continued with dasatinib – 276 (68.0)
    Follow up complete – 13 (3.2)
    Follow up on-going – 263 (64.8)

  Stopped dasatinib – 130 (32.0)
    Death whilst on study drug – 5 (1.2)
    Decision to stop drug – 125 (30.8)

Status of 125 pts who stopped dasatinib:
  - Subsequent death – 15 (3.7)
  - Follow up complete – 4 (1.0)
  - Follow up on-going – 89 (21.9)
  - Declined follow up – 16 (3.9)
  - Unknown – 1 (0.2)
## Patients who stopped study drug

<table>
<thead>
<tr>
<th>Reason for stopping study drug (exc. death)</th>
<th>Imatinib 406 (%)</th>
<th>Dasatinib 406 (%)</th>
<th>Total 812 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consent withdrawn</td>
<td>7 (1.7)</td>
<td>9 (2.2)</td>
<td>16 (2.0)</td>
</tr>
<tr>
<td>Disease progression - accelerated phase</td>
<td>1 (0.2)</td>
<td>2 (0.5)</td>
<td>3 (0.4)</td>
</tr>
<tr>
<td>Disease progression - blast crisis</td>
<td>7 (1.7)</td>
<td>4 (1.0)</td>
<td>11 (1.4)</td>
</tr>
<tr>
<td>Failure to achieve CCR after 24 months</td>
<td>4 (1.0)</td>
<td>1 (0.2)</td>
<td>5 (0.6)</td>
</tr>
<tr>
<td>Failure to achieve MCR after 12 months</td>
<td>23 (5.7)</td>
<td>3 (0.7)</td>
<td>26 (3.2)</td>
</tr>
<tr>
<td>Intolerance - non haem tox</td>
<td>53 (13.1)</td>
<td>80 (19.7)</td>
<td>133 (16.4)</td>
</tr>
<tr>
<td>Intolerance - haem/lab tox</td>
<td>10 (2.5)</td>
<td>10 (2.5)</td>
<td>20 (2.5)</td>
</tr>
<tr>
<td>Loss of CHR</td>
<td>5 (1.2)</td>
<td>0</td>
<td>5 (0.6)</td>
</tr>
<tr>
<td>Loss of MCR</td>
<td>5 (1.2)</td>
<td>2 (0.5)</td>
<td>7 (0.9)</td>
</tr>
<tr>
<td>Other reason</td>
<td>4 (1.0)</td>
<td>11 (2.7)</td>
<td>29 (3.6)</td>
</tr>
<tr>
<td>Reason unknown - Lost to follow up</td>
<td>2 (0.5)</td>
<td>0</td>
<td>2 (0.2)</td>
</tr>
<tr>
<td>‘Inadequate response’ (cytogenetic, haematological, molecular, mutation detected)</td>
<td>42 (10.3)</td>
<td>3 (0.7)</td>
<td>45 (5.5)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>163 (40.1)</strong></td>
<td><strong>125 (30.8)</strong></td>
<td><strong>288 (35.5)</strong></td>
</tr>
</tbody>
</table>
Total deaths 38/812 (4.7%)

Imatinib: 18/406 (2.2%)
- CML related 6/18 (33%)
- Non-CML related 9/18 (50%)
- Unknown 3/18 (17%)

Dasatinib: 20/406 (2.5%)
- CML related 5/20 (25%)
- Non-CML related 10/20 (50%)
- Unknown 5/20 (25%)

Other cancers: 4/9 (44%)
- Bronchogenic
- Endometrial
- Rectal
- Gastric

Non-cancer: 5/9 (56%)
- Left ventricular failure
- Bronchopneumonia secondary to emphysema
- Myocardial infarction
- Ruptured aortic aneurysm
- Bronchopneumonia

Other cancers: 3/10 (30%)
- Colon ca
- Lung ca
- Metastatic breast ca

Non-cancer: 7/10 (70%)
- Ischaemic heart disease, COPD, CCF
- Chest infection, CCF, renal failure, diabetes
- Bowel perforation
- Cardiac failure and bronchopneumonia
- Liver disease
- COPD
- Chronic cardiac failure
Outline

- Background
- Design
- What happened to all the patients?
- Progressions and deaths
- Adverse events
- Cytogenetics & PCR
- Summary
Comparative AEs

- Fluid retention
- Oedema
- Pleural effusion
- Myalgia
- Nausea
- Vomiting
- Diarrhoea
- Fatigue
- Headache
- Rash
- Pulmonary (arterial) hypertension
- Dympnoea (exertional) with no pleural effusion

Difference

95% CIs

November 2014
## Adverse events

<table>
<thead>
<tr>
<th>All grades</th>
<th>Imatinib n=406 (%)</th>
<th>Dasatinib n=406 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluid retention</td>
<td>15 (3.7)</td>
<td>12 (3.0)</td>
</tr>
<tr>
<td>Oedema</td>
<td>7 (1.7)</td>
<td>6 (1.5)</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>3 (0.7)</td>
<td>90 (22.2)</td>
</tr>
<tr>
<td>Required chest drain</td>
<td>0</td>
<td>13 (3.2)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>37 (9.1)</td>
<td>24 (5.9)</td>
</tr>
<tr>
<td>Nausea</td>
<td>131 (32.2)</td>
<td>93 (22.9)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>53 (13.1)</td>
<td>49 (12.1)</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>130 (32.0)</td>
<td>103 (25.4)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>109 (26.8)</td>
<td>131 (32.3)</td>
</tr>
<tr>
<td>Headache</td>
<td>55 (13.5)</td>
<td>103 (25.4)</td>
</tr>
<tr>
<td>Rash</td>
<td>73 (18.0)</td>
<td>108 (26.6)</td>
</tr>
<tr>
<td>Dyspnoea, no pleural effusion</td>
<td>34 (8.4)</td>
<td>65 (16.0)</td>
</tr>
</tbody>
</table>
## Cardiovascular AEs

<table>
<thead>
<tr>
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<th>Imatinib n=406 (%)</th>
<th>Dasatinib n=406 (%)</th>
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<tbody>
<tr>
<td>Arterial CV events</td>
<td>3 (0.7)*</td>
<td>9 (2.2)*</td>
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<tr>
<td></td>
<td>myocardial infarction x1, myocardial ischaemia x1, cardiac arrest x1</td>
<td>acute coronary syndrome x1, angina pectoris x4, angina unstable x1, arterial stenosis x1, intermittent claudication x1, myocardial infarction x1, myocardial ischaemia x1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>3 (0.7)*</td>
<td>8 (2.0)*</td>
</tr>
<tr>
<td>Venous events</td>
<td>4 (1.0)*</td>
<td>4 (1.0)*</td>
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*Differences not significant*
### Lab AEs

<table>
<thead>
<tr>
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<th>Imatinib 406 (%)</th>
<th>Dasatinib 406 (%)</th>
<th>Total 812 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All grades</td>
<td>Grade 3/4</td>
<td>All grades</td>
</tr>
<tr>
<td>Anaemia</td>
<td>363 (89.4)</td>
<td>101 (24.9)</td>
<td>735 (90.5)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>189 (46.6)</td>
<td>42 (10.3%)</td>
<td>401 (49.4)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>197 (48.5)</td>
<td>19 (4.7)</td>
<td>478 (58.9)</td>
</tr>
<tr>
<td>Elevated ALT</td>
<td>153 (37.7)</td>
<td>7 (1.7)</td>
<td>335 (41.3)</td>
</tr>
<tr>
<td>Elevated creatinine</td>
<td>83 (20.4)</td>
<td>13 (3.2)</td>
<td>159 (19.6)</td>
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Outline

Background
Design
What happened to all the patients?
Progressions and deaths
Adverse events
Cytogenetics & PCR
Summary
Cytogenetics at 12 months

<table>
<thead>
<tr>
<th></th>
<th>Imatinib (%)</th>
<th>Dasatinib (%)</th>
<th>Difference (%)</th>
<th>p value</th>
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<tbody>
<tr>
<td>Major cytogenetic response (MCR)</td>
<td>209/406 (51.5)</td>
<td>228/406 (56.2)</td>
<td>(4.7)</td>
<td>0.181*</td>
</tr>
<tr>
<td>Complete cytogenetic response (CCR)</td>
<td>169/406 (41.6)</td>
<td>217/406 (53.4)</td>
<td>(11.8)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Missing analyses</td>
<td>181/406 (44.6)</td>
<td>166/406 (40.9)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*caution required, missing analyses included in denominator
Definition of ‘responder’ at 12m

1. Patient remains on protocol treatment
2. PCR value available
   » Sample window extends 6 weeks either side of 12m mark
   » If no PCR taken within the sample window, values are imputed using windows A + C.
3. PCR <0.1% BCR-ABL1 / ABL1 IS [MR3]
## Imputation

### Example scenarios:
- **9 month sample A**
- **12 month sample B**
- **18 months sample C**

<table>
<thead>
<tr>
<th>Imputation applied as no 12m sample:</th>
<th>664/812 (81.8%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample B available:</td>
<td>619/664 (93.2% of 664)</td>
</tr>
</tbody>
</table>

### On treatment:
- 646/812 (80.3%)

### Actual values:

<table>
<thead>
<tr>
<th></th>
<th>Imatinib</th>
<th>Dasatinib</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No imputation needed</td>
<td>172</td>
<td>230</td>
<td>402</td>
</tr>
<tr>
<td>Imputed as “response”</td>
<td>124</td>
<td>93</td>
<td>217</td>
</tr>
<tr>
<td>Imputed as “No response” (e.g)</td>
<td>107</td>
<td>76</td>
<td>183</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Imatinib</th>
<th>Dasatinib</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No sample</td>
<td>3</td>
<td>7</td>
<td>10</td>
</tr>
<tr>
<td>No sample</td>
<td>107</td>
<td>76</td>
<td>183</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Imatinib</th>
<th>Dasatinib</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>MR3 response</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;MR3</td>
<td></td>
<td>❌</td>
<td></td>
</tr>
<tr>
<td>MR3</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
12 month PCR

Imatinib n=406

- On treatment: 320/406 (78.8%)
- Off treatment: 80/406 (19.7%)
- Unknown: 6/406 (1.5%)

Achieved MR3 Response: 175/406 (43.1%)

Δ = 15.3%  
P < 0.001

Imatinib n=406

- On treatment: 344/406 (84.7%)
- Off treatment: 59/406 (14.5%)
- Unknown: 3/406 (0.7%)

Achieved MR3 Response: 237/406 (58.4%)

Δ = 7.4%  
P = 0.001

Dasatinib n=406

- On treatment: 320/406 (78.8%)
- Off treatment: 80/406 (19.7%)
- Unknown: 6/406 (1.5%)

Achieved MR4.5 Response: 24/406 (5.9%)

Total Cohort n=812

- On treatment: 344/406 (84.7%)
- Off treatment: 59/406 (14.5%)
- Unknown: 3/406 (0.7%)

Achieved MR4.5 Response: 54/406 (13.3%)

Δ = 7.4%  
P = 0.001

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### PCR response and pleural effusion

<table>
<thead>
<tr>
<th></th>
<th>Imatinib n=406</th>
<th>Dasatinib n=406</th>
<th>Total n=812</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCR &lt;0.1% (MR3)</td>
<td>175 (43.1%)</td>
<td>237 (58.4%)</td>
<td>412 (50.7%)</td>
</tr>
<tr>
<td>No pleural effusion</td>
<td>403</td>
<td>316</td>
<td>719</td>
</tr>
<tr>
<td>PCR &lt;0.1% (MR3)</td>
<td>174 (43.2%)</td>
<td>*178 (56.3%)</td>
<td>352 (49.0%)</td>
</tr>
<tr>
<td>With pleural effusion</td>
<td>3</td>
<td>90</td>
<td>93</td>
</tr>
<tr>
<td>PCR &lt;0.1% (MR3)</td>
<td>1 (33.3%)</td>
<td>*59 (65.6%)</td>
<td>60 (64.5%)</td>
</tr>
</tbody>
</table>

*Difference not significant*
## Partial PCR responses

<table>
<thead>
<tr>
<th></th>
<th>Imatinib</th>
<th>Dasatinib</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>3 month PCR samples available</strong></td>
<td>317 (100%)</td>
<td>319 (100%)</td>
<td>636 (100%)</td>
</tr>
<tr>
<td>PCR &gt; 10% (MR1) at 3 months</td>
<td>66 (20.8%)</td>
<td>20 (6.3%)</td>
<td>86 (13.5%)</td>
</tr>
<tr>
<td>PCR &lt; 10% (MR1) at 3 months</td>
<td>251 (79.2%)</td>
<td>299 (93.7%)</td>
<td>550 (86.5%)</td>
</tr>
<tr>
<td><strong>12 month PCR samples available</strong></td>
<td>210 (100%)</td>
<td>267 (100%)</td>
<td>477 (100%)</td>
</tr>
<tr>
<td>PCR &gt; 1% (MR2) at 12 months*</td>
<td>20 (9.5%)</td>
<td>10 (3.7%)</td>
<td>30 (6.3%)</td>
</tr>
<tr>
<td>PCR &lt; 1% (MR2) at 12 months*</td>
<td>190 (90.5%)</td>
<td>257 (96.3%)</td>
<td>447 (93.7%)</td>
</tr>
<tr>
<td><strong>Total with 'less than ideal' progress</strong></td>
<td>86/317 (27.1%)</td>
<td>30/319 (9.4%)</td>
<td>116/636 (18.2%)</td>
</tr>
</tbody>
</table>
PCR data: all patients, both arms

7,431 data points, IS
11 patients who ‘died from CML’

- 3 overt blast crisis
  - 10.6 month interval to death
  - 12.6 months
  - 14.2 months
- 1 equivocal accelerated phase
  - 42.4 months
Outline

Background
Design
What happened to all the patients?
Progressions and deaths
Adverse events
Cytogenetics & PCR
Summary
SPIRIT 2 summary

• Largest investigator-conducted randomised trial of dasatinib vs imatinib
  – n=814
  – median follow up 3 years

• Both drugs generally well tolerated
  – 512 of 812 (62.9%) continue on study medication
  – Imatinib: GI tox; Dasatinib: pleural effusions, headaches
  – No difference in cardiovascular events

• MR3 rate at one year is: imatinib 43%, dasatinib 58%

• 774/812 (95.3%) remain alive overall
  – imatinib 388/406 (95.5%); dasatinib 386/406 (95.0%)

• No difference in progression or overall survival
An NCRI randomised study comparing dasatinib with imatinib in patients with newly diagnosed CML


www.spirit-cml.org
## Comparison with Dasision

<table>
<thead>
<tr>
<th></th>
<th>Imatinib (%)</th>
<th>Dasatinib (%)</th>
<th>Difference (%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dasision(^1,^2)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MR(^3) at 1 year(^1)</td>
<td>28</td>
<td>46</td>
<td>18</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>MR(^3) at 3 years(^2)</td>
<td>55</td>
<td>69</td>
<td>14</td>
<td>&lt;0.0001</td>
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<tr>
<td><strong>SPIRIT 2</strong></td>
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<td></td>
</tr>
<tr>
<td>MR(^3) at 1 year</td>
<td>43</td>
<td>58</td>
<td>15</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

\(^1\)Kantarjian et al. NEJM (2010); 362:2260  
\(^2\)Jabbour et al. Blood (2014); 123: 494-500  
*rates are KM cumulative incidence  
See also Cortes et al. Abstract 154