COVID-19 and Cancer Clinical Trials

James, H. Doroshow, M.D.

1st Virtual Joint Meeting of NCI Board of Scientific Advisors & National Cancer Advisory Board

April 9, 2020

COVID-19 and Cancer: Some Numbers from Wuhan

- Gender: ~70% male
- Death rate overall: >10%
- ICU admission rate: >15%
- Increased mortality: patients with lung, GI, metastatic cancer

Appreciate the health professionals in cancer centers and in both inpatient and outpatient facilities caring for cancer patients with this virus.

NCTN Accrual for "Intervention" Step in Trials by Lead Group & Week: 2-3-2020 to 3-29-2020 (CTSU Open Data)

Intervention / Cohort Step Enrollments	2/3-2/9	2/10-2/16	2/17-2/23	2/24-3/1	3/2-3/8	3/9-3/15	3/16-3/22	3/23 to 3/29	% Change Last Week Vs Avg of 7 Prior Weeks
ALLIANCE	93	88	83	93	105	94	67	30	**-66%**
CCTG	2	5	5	4	6	3	6	4	**-10%**
COG	43	53	47	45	51	58	41	34	**-30%**
ECOG-ACRIN	45	56	47	51	45	45	43	35	**-26%**
NRG	44	57	44	59	45	46	49	24	**-51%**
SWOG	49	46	43	54	54	46	54	35	**-29%**
TOTAL	276	305	269	306	306	292	260	162	**-44%**

NCTN Accrual for "Screening" Step in Trials by Lead Group & Week: 2-3-20 to 3-29-20 (CTSU Open Data)

Screening Step Enrollments	2/3-2/9	2/10-2/16	2/17-2/23	2/24-3/1	3/2-3/8	3/9-3/15	3/16-3/22	3/23 to 3/29	% Change Last Week vs Avg of 7 Prior Weeks
ALLIANCE	24	22	25	28	22	27	13	7	**-70%**
CCTG	7	10	18	10	6	10	6	11	**15%**
COG	9	14	14	9	5	9	9	5	**-49%**
ECOG-ACRIN	17	9	15	14	15	16	13	6	**-58%**
NRG	13	5	9	6	8	7	13	2	**-77%**
SWOG	20	28	28	23	30	24	23	21	**-16%**
TOTAL	90	88	109	90	86	93	77	52	**-42%**

COVID-19 and Cancer Clinical Trials

- Some institutions have shut down accrual to most studies; volume of COVID-19 patients has overwhelmed ability to provide care (NYC)
- Several have not: UCSF, NIH clinical center, others: trial accrual continues where staff available to treat those patients:
  - ✓ who need curative therapy or who have no viable options beyond a clinical trial
  - ✓ with clear potential for therapeutic benefit
  - ✓ suggest limiting accrual for non-therapeutic studies

NCI's Clinical Trials Networks: Response to COVID-19

- Modifications to NCI clinical trial processes
- Tocilizumab compassionate use study
- National COVID-19 natural history study

NCI Adapting to COVID-19 (1)

- Patient care can be transferred to different participating study sites
- Local healthcare providers can provide study activities to provide continuity of care (oversight by responsible investigator)
  - ✓ Treatment with non IND drugs
  - ✓ Physical exams, KPS, overall assessments
  - ✓ Protocol-specific clinical lab tests
  - ✓ Protocol-specified blood collections
  - ✓ Protocol-specified radiologic imaging, EKG's, cardiac ultrasound
- NCI can ship oral IND agents directly to patients—including potential to ship multiple cycles of drug; dispensing pharmacies at sites can also ship drugs directly to patients (exceptions for agents considered 'dangerous goods' by US Dept. of Transportation; dasatinib, TAK-228, few others)

NCI Adapting to COVID-19 (2)

- Injectable CTEP IND agents must be administered at a registered site (FDA)
- Alternative procedures that do not compromise safety or the integrity of the study will be considered minor deviations:
  - Documented in the medical record with reason (ie., travel restriction)
  - Include: study visits by telemedicine rather than in-person; delayed study visits; delayed lab or imaging tests; minimal treatment delays; biospecimen collections
- Major deviations may be unavoidable; must still be reported to CIRB
- On-site auditing visits are being re-scheduled; remote auditing has been adopted by NCTN groups
- NCI CIRB supports “remote” informed consent: telephone discussion in conjunction with patient signature on written document

Compassionate Use Protocol for Tocilizumab

"Tocilizumab in Hospitalized Cancer Patients with Coronavirus 2019 (SARS-CoV-2) And Severe Complications of Corona Virus Disease 19 (COVID-19)"

- NCI will use its **treatment referral (compassionate use)** mechanism to distribute tocilizumab to cancer patients with incipient respiratory compromise based on potential role of IL-6 in etiology of COVID-19-related ARDS
- Protocol developed by Dr. Rich Little (CTEP) and Dr. Nirali Shah (POB) in 4 days; final negotiations ongoing with Genentech for study to accrue 200 patients (age >2 yrs) with broad eligibility criteria that include severe respiratory compromise from presumed or proven COVID-19 infection. For patients in ICU or about to move to ICU, or worsening lung function in ICU.
- **Goal**: Decrease time in ICU, time on ventilator, time in hospital
- Collect limited clinical data set and blood for biomarker evaluation
- Activate across NCI clinical trials networks in institutions that are not participating in Genentech's phase III trial of agent

NCI Cancer and COVID-19 Longitudinal Cohort

- NCI building a >2000-patient (sample size estimates ongoing) US national cohort of cancer patients with COVID-19 at > 1000 sites across the NCTN, ETCTN, NCORP, and NCI-designated Cancer Centers to include high, moderate, and currently low prevalence regions; full per case reimbursement from NCI; need to enroll from minority NCORP sites
- NCI infrastructure for development and execution of a natural history study: electronic case report forms, clinical trial documents, banking of blood specimens, NCI CIRB
- Collaborative extramural/NCI leadership team to oversee COVID-19 and Cancer Working Group: clinical trialists, statisticians, epidemiologists, virologists, clinical geneticists, informaticians
- **GOALS**: 1) Cohort of cancer patients infected with COVID-19 comprising all age groups for collection a comprehensive dataset on the cancers, treatments, medications, symptoms, course, and recovery, and co-morbidities with longitudinal follow-up every 1-2 mo until return to pre-morbid status; 2) Follow subset of pts for > 1 yr to assess impact of COVID-19 on survivorship and QOL; and 3) Collect blood samples at study entry and then every 2 mo for 1 yr to estimate antibody response, genetic susceptibility, and for biomarker development; collect blood from family members; 4) Public database/biospecimens

NCI Cancer and COVID-19 Longitudinal Cohort (2)

Critical Study Milestones:

- Initiate patient accrual before May 15, 2020: **from idea to active trial in < 6 weeks**
- Enroll the first 500 patients within 3 months of trial activation
- Complete accrual of 2000 patients nationwide by 12/1/2020
- Complete follow-up and survivorship evaluations by end of 2021
- Begin biomarker studies on blood samples soon after initial 500 patients accrued

COVID-19 and Cancer Clinical Trials: Other Critical Activities

- More than a dozen NCI-Designated Cancer Centers have developed their own therapeutic trials for cancer patients with COVID-19
- Vanderbilt CCC initiated a grassroots effort to collect clinical data on cancer patients with COVID-19 infections based on a set of de-identified information; uses an open access, internet database that is now endorsed by >70 Cancer Centers, hospital systems, and large practices: *The COVID-19 Cancer Consortium.* Opened 3/30/2020
- Large pharma (Roche/Genentech; Amgen; others) has initiated several phase III trials of IL-6R antibodies, antivirals in cancer and non-cancer patients with COVID-19

Appreciation

Demonstrates the potential for NCI—working its grantees—to flexibly make use of its clinical research infrastructure in a time of national emergency

CTEP
Meg Mooney, Larissa Korde, Andrea Denicoff, Rich Little
DCP
Worta McCaskill-Stevens, Paul Pinsky, Marge Good
DCCPS
Robert Croyle, Paul Jacobsen
DCEG
Stephen Chanock
CCR
Bill Dahut, Nirali Shah

Vanderbilt Univ. Comprehensive Cancer Center
Brian Rini, Jeremy Warner

Discussion